# TRANSACTIONS

OF

# The Association of Life Insurance Medical Directors of America

FIFTY-EIGHTH ANNUAL MEETING

James R. Gudger, M. D.
*Editor*

VOL. XXXIII

PRESS OF
Recording & Statistical Corporation
New York City
1950

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# Transactions
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## FIFTY-EIGHTH ANNUAL MEETING

The Fifty-eighth Annual Meeting of The Association of Life Insurance Medical Directors of America was held at the Hotel Statler in New York City on Thursday and Friday, October 13 and 14, 1949.

PRESIDENT DEWIS—It gives me a great deal of pleasure to welcome you to our Fifty-eighth Annual Meeting. This occurs at a time when our Association has attracted international interest, as manifested by its indirect participation in the recent Congress in Rome and by the fact that we have now changed our Constitution to permit applications for membership from medical directors of insurance companies outside the United States and Canada. As you know, we have just elected five of these gentlemen to membership, and I hope that as time goes on they will be joined by others and that our foreign associates will find it possible to join with us actively in these meetings.

I am sure you will agree that our committee has provided us with an excellent scientific program to which we will hasten without further preliminary remarks on my part. However, before proceeding, I do think that we would like to have a few words from Dr. Ennion S. Williams, Medical Director of the Life Insurance Company of Virginia and Chairman of the Medical Section of the American Life Convention. I am pleased to introduce Dr. Williams.

DR. WILLIAMS—On the train coming to the meeting I made a comparison of the roster of the Medical Section of the American Life Convention and the membership of this organization. I find that ninety per cent of the members of the

Medical Directors Association belong to the Medical Section of the American Life Convention. To that ten per cent who do not belong to it, on behalf of the Medical Section I wish to extend a cordial invitation to attend the meetings of the Medical Section, especially the meeting of next June.

Those meetings have the same purpose as does this meeting but they differ in one respect. At the Medical Section meetings, all afternoon work must be accomplished in a rocking chair on the veranda, on the golf course, or in the swimming pool.

For the ninety per cent who do belong to the Medical Section, I wish to inform you that the next meeting will be held at the Greenbriar Hotel, White Sulphur Springs, June 15, 16, and 17. The Secretary has made excellent arrangements. The Program Chairman is working hard. If you have any suggestions to give him, he still may squeeze in a few more subjects. I will repeat that date, if you want to write it down—June 15, 16, and 17. Thank you.

PRESIDENT DEWIS—We are happy to have with us this morning Dr. Francis R. Dieuaide, the Scientific Director of the Life Insurance Medical Research Fund, who, I hope, will be willing to say a few words to us at this time.

DR. FRANCIS R. DIEUAIDE—This coming December the Research Fund will be four years old. In 1949 the sum put at the disposal of the Fund for its purposes was about $700,000.

Since the establishment of the Fund the member companies have contributed through it over two and a half million dollars to research on diseases of the heart and circulation. Support has been given by the Fund to one hundred and twenty-eight research programs in this vital field, and, in addition, fellowships have been given to seventy-eight young men and women to enable them to become investigators of cardiovascular problems.

The research aided by the Fund has been distributed among seventy-four institutions, which are located in twenty-nine of our states, in four Canadian provinces, and two foreign

countries. The results of this work have been described by the investigators in over four hundred fifty medical articles. Copies of most of these articles have been distributed to the medical directors of member companies. I might say in passing that we realize full well that the majority of these articles are highly technical. In view of the policy of the Fund, it is proper that they should be, because our main efforts are being directed at fundamental work. Included in the group, however, are a number of articles of general interest and, I think I may say, obvious importance. The number of such articles will increase as time goes on, and the now separate pieces of research will coalesce and give rise to broader conclusions.

It is impossible for me to summarize here the great volume of work which is described both in detail and in summary in the Fund's annual reports which all of you receive regularly. The promising available leads to causes of arteriosclerosis and hypertension are all being studied, including especially dietary, metabolic, hormonal and psychological factors. Several important programs are devoted to rheumatic fever and it is of special interest to us that one of the Fund's Fellows, a young man who has been a Fellow for three years now, has made a very important contribution to the etiology of rheumatic heart disease.

Some of the programs are devoted to improvements in diagnosis and treatment, but they are a minority of the total because of the general policy I mentioned before, which we believe is a wise one, of devoting most of the available support to basic work. Only the results of such investigations can provide the necessary basis for the development of methods of preventing arteriosclerosis, hypertension, and rheumatic heart disease, which is what we all have in mind, of course, as the ultimate desideratum.

Investigators have shown their appreciation of the Fund's support in many ways, particularly in the continued number and quality of their requests for help. Only one out of four or five of the requests received can be granted, because of the limitation in the volume of support which we can give. This

point, of course, needs to be borne in mind when you hear complaints of our not having made grants in response to requests. It will be agreed upon by all that it would not be desirable for us to be able to grant all the requests we receive. When I say that we are able to grant only one in four or five of those we receive I am referring to reasonably good requests; I am not including the fringe requests which do not need consideration because they are outside our field or obviously do not make much sense.

We have had a total of over seven hundred and fifty applications to consider and I can assure you that all requests which do come within our field and do make some sense are given thorough consideration. So far there has been no indication whatsoever of a slackening of demand for support by the Fund.

The establishment and devotion of the Fund to the problems of heart disease was and is a great stimulus to work in this field, which, as you all know, was previously woefully neglected. There has already been a great increase in the number of qualified workers who are putting their efforts into cardiovascular problems. In this connection we are especially proud of the fellowship program of the Fund because the men who have held fellowships are making an excellent record. This, of course, is the result of their own work, but it speaks well for the selection of the men to whom these fellowships have been given. A number of the men who had the first fellowships given by the Fund already have posts of substantial importance in teaching and investigation.

This year the Federal Government provided a substantial sum for research in this field. Actually it amounted to about three million dollars, and not ten million dollars, as some of the press announcements may have suggested. This money was all absorbed by the day after its availability, namely, the first of July, 1949.

The role of the Fund continues to be a vital one, because in a unique way it can fill the function of insuring preservation of the spirit of free enterprise, which is nowhere more essential than in research.

PRESIDENT DEWIS—Thank you very much, Dr. Dieuaide. Gentlemen, we now come to the scientific portion of our program, the first paper of which is entitled "Rickettsial Diseases in the United States," by Dr. William S. Middleton, Professor of Medicine and Dean of the Medical School of the University of Wisconsin and President-elect of the American College of Physicians.

Dr. Middleton has had a very active career in medical education and science and, during the recent World War, served with great distinction as Chief Consultant in Medicine in the European Theatre of Operations of the United States Army, having the rank of Colonel. He is a member or fellow of numerous professional organizations in this country and abroad and is very well known among internists for his work as secretary-treasurer of the American Board of Internal Medicine during the busy years of its development. Dr. Middleton, it is a great pleasure to welcome you, sir.

# RICKETTSIAL DISEASES IN THE UNITED STATES

WILLIAM S. MIDDLETON, M. D.
*Dean and Professor of Medicine*
*University of Wisconsin Medical School*
*Madison, Wisconsin*

For many years rickettsial disease was considered exotic and entirely foreign, almost academic in our routine considerations of diseases. With the conquest of the bacterial infectious diseases there is increasing emphasis upon viral and rickettsial diseases and, reviewing the situation carefully, it becomes apparent that we are having an increasing contact with and responsibility for the control of rickettsial diseases.

The rickettsial bodies stand midway between bacteria and viruses. They are interesting pleomorphous organisms, gram-negative in reaction, requiring the presence of living tissue for their cultivation outside of the body. Within the body they occupy intracellular positions. In nature there is usually a well recognized reservoir, and for their transmission there is necessary the presence of a biting insect. In the immunologic reactions there is again a wide range of similarity. Before the Rickettsiae were recognized as etiologic agents, the Weil-Felix reaction, the agglutination of the B. proteus by the serum of patients suffering from rickettsial diseases was a common finding. Indeed, these reactions are now recognized as nonspecific but they are none the less interesting and widespread. Cross immunity is not known except between certain of the true typhus group, endemic and epidemic, and the tick-borne South African type.

By reason of the importance of this subject, classification has been attempted and Megaw, for the British, used the vector as the differential agent; in other words, he said it was much better to classify according to louse, flea, tick, mite typhus. This simplification has not proved particularly effective, and we are led to differentiate on distinct bases, both clinically and epidemiologically.

The pathology of these rickettsial diseases is singularly common to all. There is a histologic unit, namely an infectious vasculitis. The appearance of a small arteriole in the skin in a patient suffering from epidemic typhus fever may be taken as a type (Fig. 1). There is an intimal injury and hyperplasia of intimal endothelium. A perivascular, round-cell infiltration with plasma cells, mononuclear cells, and lymphocytes, in the main further characterizes the process. Because of the injury to the intima, there is a peculiar tendency for thrombosis.

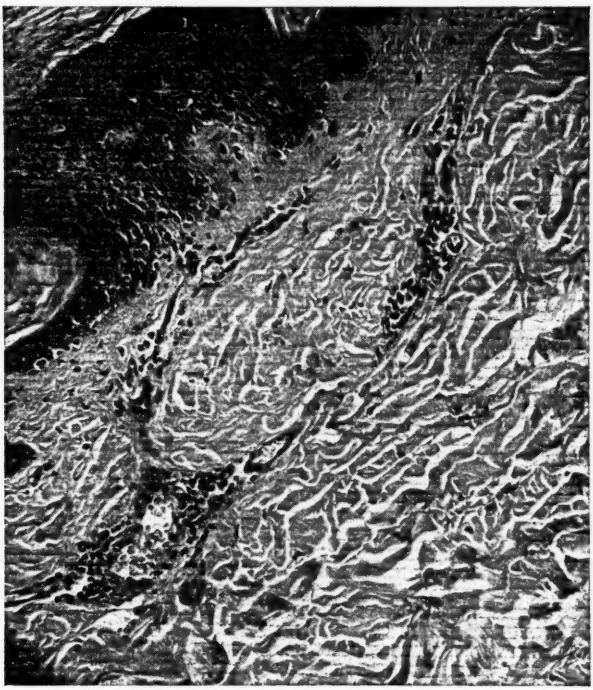

Fig. 1. Histological appearance of the skin in epidemic typhus fever.

If you bear in mind this histologic unit of pathologic change, we may apply it to the clinical pictures of these several diseases. Historically, the most interesting among these is, of course, typhus fever (the synonyms for which will give the connotation of crowding and filth), known in the past as putrid fever, jail fever, ship fever, starvation, or famine fever, caused by two Rickettsiae, dependent upon its type. The *epidemic* form is caused by the Rickettsia prowazeki, the name dignifying two medical martyrs to the study of the disease, Ricketts, the American, Prowazek, the Pole. This organism has an intermediate phase in the body louse. The life cycle is R. prowazeki, in the body louse, to man, to louse, to man, to louse. From the standpoint of epidemiological control, there is an interesting circumstance. Ten days of growth in the gastrointestinal tract of the louse must elapse before the louse becomes infective. Bear in mind that ten days' grace period. The intermediate host, or the reservoir, is the human being, a most significant detail. The manner of communication is not the transmission through the saliva of the louse but rather the irritation caused by the louse, whereupon the human subject rubs the Rickettsia from the dejecta of the louse into minute abrasions in the skin.

The *endemic* form of typhus fever is caused by the Rickettsia mooseri. In this instance the flea is the vector; the reservoir is the rat—to flea, to rat, to flea. The human being is off on a dead-end street—that is to say, there is no further communication or communicability from this source.

These two diseases have distinct common parts in clinical manifestation—an incubation period usually of from eight to twelve days, the shorter period in the case with the endemic form. The first manifestations are those of chilling, general malaise, aching, headache, backache, weakness. Then in about the fourth to fifth day of the febrile period, there appears an eruption which is usually forecast by the appearance of "the morning after the night before." The face is bloated, the vessels of the face stand out rather prominently, and it is rather edematous. The eruption, however, does not appear in the face but on the trunk, along the axillary folds, the

thorax, and the abdomen. It is first macular and then becomes, in a period of about two days, or on the seventh day of the disease, definitely petechial and can no longer be obliterated by pressure. This eruption continues throughout the height of the disease to fade and perhaps thereafter to leave mottling or areas of slight pigmentation, marked on hyperemia, with exertion or increased temperature. The constitutional reaction is marked by the febrile rise in step-like fashion until about the third day when a fastigium of 102 F. to 105 F. is reached. This is held for ten to twelve days and lysis occurs in a period of two days, rather rapid, to normal. Occasionally there are recrudescences or relapses. Prostration is marked. The mental attitude of the patient reflects the meningeal and central invasion of the Rickettsiae. The flushing of the face, suffusion of conjunctiva, miosis of pupils, and delirium, giving way to coma (the term "typhus" means coma) are significant manifestations. Splenic enlargement may be established in the first week.

This condition may be complicated by cardiac failure, uremia, bronchopneumonia, and thrombosis. Gangrene may occur in dependent areas, particularly about the scrotum, the prepuce, sometimes the buttocks, tip of nose, tips of fingers, and ear lobes.

From the laboratory standpoint, importantly a leukocytosis of 12,000 to 15,000 is found. The monocytes are increased relatively and absolutely. The Weil-Felix reaction (OX–19) becomes positive at the end of the first week, or into the second week. Because of its nonspecificity, there have been applied agglutination, complement fixation, and neutralization tests in more recent years. They do not anticipate the diagnosis. There has been recourse to biopsy at times with this idea in mind, and the histologic unit in the skin is characteristic.

For clarification in relation to a modified form of the typhus fever, a word regarding Brill's disease. In the September 29, 1949, *New England Journal of Medicine,* a paper by Blumberg, Doane and Weiss, of Philadelphia, cited three patients who had had typhus fever in Russia years ago and had suffered

the recrudescence that is known as Brill's disease. For this definition of the relationship of Brill's disease to epidemic typhus fever, we are indebted to Hans Zinsser. Twenty to thirty years removed from the initial attack, there may be a recrudescence in this country. It inevitably occurs in individuals who have emigrated from countries where epidemic typhus exists, and its manifestations are considerably milder. The same holds true of endemic typhus fever.

The further laboratory determinations that are important in prognosis are the low serum protein, usually a sacrifice of the serum albumin, and the rising nonprotein nitrogen. Indeed, from a prognostic standpoint, in the experience of the Mediterranean Theatre, the rising nonprotein nitrogen was the most important detail in the study of typhus fever.

One of the rickettsial diseases with a geographic name that is not particularly well borne out by fact, is Rocky Mountain spotted fever, caused by the Dermacentroxenus Rickettsia, or the Rickettsia rickettsi. This disease is not confined to the Rocky Mountain states; as a matter of fact, it has been reported in forty-three states in the Union. Maine, Vermont, Rhode Island, Connecticut, and Michigan are the only five states in which indigenous infection has not been reported.

The vector for this Rickettsia is the tick, the wood tick, or the Dermacentor andersoni in the Far West, the Rocky Mountain area, and the Dermacentor variabilis or dog tick for the East; that is, the wood tick for the West, the dog tick for the East. This very circumstance gives you a clue as to the difference in the epidemiology. It will affect outdoor men, herdsmen in the West, particularly in the grazing season which begins in April and May. In the East, because of the dog tick vector the incidence will be later, June and July, and the people involved are those in contact with dogs, more commonly children and women. There is a further interesting circumstance of mortality figures. In the Bitter Root Valley, a mortality of 80 per cent obtains, whereas in the Snake River Valley there is a mortality of only 5 per cent. The Indians grazing their stock in the days before the white man's invasion of this area shunned the Bitter Root Valley at

certain seasons for this very reason. The life cycle is tick, rodent, tick, rodent—man is off on a dead-end street again. In the life of the tick, it is necessary that it go through three feeding periods, two on small mammals and one on large mammals, before it can communicate the disease. Furthermore, it is possible for the Rickettsiae to pass from tick to the larva without going through these intermediate stages, so that infection may be running right through strains of the ticks themselves; but before they can transmit the disease, they must have the support or nourishment of mammalian blood.

The inception of the disease after an incubation period of five to eight days is very much more fulminating than that of the true typhus fever, epidemic or endemic, a sharp rise in twenty-four to forty-eight hours to temperatures of 103 F. to 105 F., extreme prostration, headache, nosebleed, backache, generalized malaise. Weakness is conspicuous; the mental symptoms are outstanding. The eruption, usually the second or third day of the disease, begins about the wrists and ankles, spreads to involve the entire body, and, unlike typhus fever, there is involvement of the face and hands. The eruption goes on to a hemorrhagic stage very early. Desquamation succeeds, as a rule. Quite frequently, in addition to the subcuticular mottling there is a maintained pigmentation that becomes marked when there is vasodilatation. The constitutional symptoms of these patients are quite marked. Prostration advances. The central nervous manifestations of delirium and coma are common. Miosis, as in typhus, is again seen. The temperature that has ranged from 103 F. to 105 F. usually wider swings than in typhus fever, will run a course of two to three weeks and then subside to normal by slow lysis over a period of three to seven days. The pulse is usually disproportionately rapid and the respiratory rate increased.

Myocardial injury may result in a fatal outcome. There may be renal complications, thrombosis and gangrene of the peripheral areas, as lobes of the ear, tip of nose, finger tips, soft palate, scrotum, prepuce, buttocks, and vulva, gangrene being much more common than in the typhus of the endemic or epidemic types.

The laboratory returns include a leukocytosis of 12,000 to 15,000 with mononuclear increase. The Weil-Felix reaction is positive (OX19 and OX2) in Rocky Mountain spotted fever. There are positive tests for agglutinins, complement fixation and neutralization of the virus. The low serum protein is noted. Albumen, red blood cells, and a few casts may be found in a highly concentrated urine. Azotemia is ominous. The occasional instance of myocardial injury with conduction faults in the electrocardiogram should be borne in mind.

The next of the rickettsial diseases of interest to us, incidentally but not locally, is tsutsugamushi or scrub typhus fever that so plagued our troops in certain areas of the Pacific. It is caused by the Rickettsia tsutsugamushi. The vector is a mite, the intermediate host rodents; hence back through the mite, to the rodent, to the mite, with man again on a dead-end street. He was afflicted only if he went through kunai grass at the time there was abundance of the larvae on the same. This disease is interesting to us in two respects, first as an agent in mortality; nine per cent of the affected, in the Pacific area, died largely from cardiac failure. Second, in the prospect of the initiation of vascular injury, that may give belated manifestations among those affected after a period of years. This project should interest our Army and our Veterans Administration until they can give an answer to the ultimate reflection of this injury in future disability.

Another among these diseases that does not interest us particularly today is trench fever, an old adversary of which we saw much in World War I. It is caused by Rickettsia quintana. The vector is the body louse in all probability. The reservoir is not known. The mortality was negligible. The morbidity was particularly great. The British figures are simply astounding. During World War I, 45,000 per million troops per year in the British Expeditionary Force in France were affected. Of this number, 90 per cent were disabled for upward of three months. If we accept these figures, the attrition in man power from trench fever in World War I was stupendous. Interestingly, in the interval between World War I and World War II there were two laboratory epidemics

of very limited order. In World War II we were prepared for trench fever but did not see it in our forces. It was reported from the Near East and the Balkans in sporadic epidemics.

The Australian Q fever has come to us in interesting guises. Queensland is the basis for the initial Q, and the cycle is from tick to bandicoot, to tick, to bandicoot, to tick—with the cow and human being off on the side. The Rickettsia burneti is the responsible etiologic agent. The occurrence of a peculiar epidemic in North Africa, repeated in the Italian campaign, led to studies in this country that fixed the Rickettsia burneti as the cause, and Q fever was the diagnosis. We have had three epidemics in this country in recent years. Topping reported its occurrence among stock handlers at Amarillo, Texas. Shepard gave a splendid account of an epidemic in Chicago in the *American Journal of Hygiene* for September, 1947. Both experiences were among stock handlers or butchers. A further incidence is cited in Oakland, California. The life of the tick is not essential. Indeed, no American instance of such a vector is recorded. Reviews of the milk shed for Los Angeles indicate that the cattle, perhaps sheep and goats, in that area are affected by this form of Rickettsia. The Rickettsia have been isolated from the milk there and of course constitute a particular and peculiar charge in public health control.

The pathology of this condition differs in an essential detail from the others in that the focal point is an interstitial pneumonitis with infiltration by monocytes and some monocytic transudation into the alveoli. After an incubation period of nineteen to twenty-five days, which has been best measured in people accidentally infected in the laboratory, there is a rise in temperature, malaise, backache, and cough. The cough occasionally may be productive of blood but usually is harsh, racking, and totally unproductive. A slight macular eruption may be observed, but it is evanescent and has not been well defined in location. Occasionally the spleen is enlarged. At times crackling rales, after the pattern of viral pneumonia, may localize the pulmonary process; but we are struck by the fact that in spite of the minor constitutional manifestation,

the temperature rarely rising above 101.5 F., x-ray of the chest will show disproportional, patchy pneumonia.

The laboratory aids besides the x-ray include a leukopenia or low leukocytosis. There is no Weil-Felix reaction in Q fever; however, there are agglutinins for the Rickettsia burneti. The serum of the patient will agglutinate the cultures of Rickettsia burneti. Antigens from Rickettsia burneti will give complement fixation tests in the serum of the patient. In passing, it must be said that of all the rickettsial diseases we must be most on guard for detection, diagnosis, and control of Q fever. The mortality has been very low. In death from this cause, a very extensive bronchopneumonia has been the background. Complications of pleural effusion, arthritis, orchitis, and epididymitis are infrequent.

Not to be outdone, of course, Texans would have a disease of their own. A unique condition was reported by Woodland, et al, in the *Journal of The American Medical Association* of August 21, 1943. About 500 patients were admitted to the Station Hospital of Fort Sam Houston, within a period of two months, from Camp Bullis, Texas. These soldiers had been subjected to the bites of many insects, and, for poetic license, it was the Lone Star tick that was determined as the offending vector. The patients suffered from extreme prostration, headache, anorexia, malaise, chills, fever, weakness, and went on to a rather debilitating course, ranging from four to fourteen days and averaging five days. The temperature rose from 101.5 F. as high as 105 F. The debility of these patients was disproportionate to any clinical manifestations. A mild eruption, macular in type, marked most of these. There was a remission usually about the second or third day, with a relapse. This remission was of the saddle back type; so we have Texas complete—the Lone Star tick, the saddle back type fever, Bullis fever.

There were no deaths. Hence the pathology is unkown. The laboratory procedure showed leukopenia of unusual degree, down to 1,750 white cells and as few as 23 per cent neutrophiles. There was a real neutrophilic depression and the monocytes and the lymphocytes were relatively increased.

The Weil-Felix reaction was universally negative. The tests for the agglutination of an isolated organism (rickettsial in morphology), grown on the chick embryo allantoic membrane, were positive. Complement fixation with the antigen prepared from this group was positive in the serum of the patients suffering from the disease. Bullis fever may be a chance rickettsial disease. Certainly it is entirely different from Q fever, viral pneumonia, Rocky Mountain spotted fever, the Colorado tick fever, and other confusing details.

One of the most fascinating of rickettsial diseases was first encountered among dwellers near a building operation in metropolitan New York in June, 1946. The best account of this newcomer, rickettsialpox, is the report of Greenburg, Pellitteri, Klein, and Huebner, in the March 29, 1947, *Journal of The American Medical Association.* The cause of this rickettsial disease is the Rickettsia akari. The life cycle is from a mite to a mouse, to a mite to a mouse. Again man is on the dead-end street.

The mite that has been infested with the Rickettsia bites the human subject. At the site of the bite, a firm papule appears. In turn, this becomes a deep-seated vesicle and eventually an eschar. There is regional lymphadenitis. This cycle develops about seven days before the constitutional reactions which are those of the general infection with headache, backache, general malaise, aching in the bones, and profuse sweating. The temperature is not inordinately high, 101 F. to 103 F. The febrile period may last from 3 to 17 days. Fall to normal by lysis is the rule. There is a tendency for remissions and relapses. About the third or fourth day a generalized eruption like chickenpox appears. The initial deep-seated papule becomes vesicular. The contained clear fluid changes to a turbid one. Umbilication and crusting succeed. This is usually a sparse eruption and involves any portion of the body except the soles of the feet and palms of the hands. It has been described in the mucous membrane of the mouth. None of these patients has died.

The blood count shows leukopenia from 2,400 to 7,500. The Weil-Felix reaction is negative. There is agglutination of the

cultured Rickettsia akari by the serum of these patients, and complement fixation by the antigen prepared from the Rickettsia akari is diagnostic. Incidentally, we have little reason to feel that this disease is so localized in its distribution as the reported instances from metropolitan New York.

If we retrace our steps, it becomes apparent that we have a series of diseases and, knowing their etiology, we have a target for attack in preventing their spread; knowledge of the reservoir is a further method of control and beyond that specific measures of direct assault. Considering the vectors first, these are the louse, the flea, the tick, the mite, all of which are targets, some of which are very susceptible to insecticides, most of them very definitely vulnerable to repellent agents. In Rocky Mountain spotted fever, the handling of the tick must be most cautious to avoid preventable infection. First of all, individuals are clothed to protect the body against the invasion of the tick. They should inspect their skin twice a day to be sure that the tick has not lodged. It takes the insect about four hours to have its meal of blood. Then, if a tick is found engorged, do not squash it on the body but remove it with a metal tweezers or with a glove and destroy by fire or other method. Care must be observed not to squash it in the hands, as this may result in infection. Fortunately DDT is not only repellent but also an insecticide against the louse, the flea, and the mite.

Next let us consider the reservoir. Unfortunately, the reservoir for epidemic typhus fever is man. The rat, the rodent, the bandicoot, the mouse, the reservoirs for the respective Rickettsiae that have been discussed, can and should be eliminated in the control of these rickettsial diseases. When we come to the dead-end group where man is affected incidentally, there is always a chance of getting a double pass here behind the line of scrimmage. We may definitely hope, in the case of the endemic typhus fever, Rocky Mountain spotted fever, Q fever, and rickettsialpox, to interrupt the cycle at one of two points, either with the vector or with the mammalian reservoir, before man is exposed to these.

Reference has been made to an interesting grace period. This was particularly demonstrated in recent experience in the European Theatre in the ability to interrupt epidemics, but most spectacularly in the experience in Naples in the Mediterranean Area. Here there was rampant an epidemic of typhus fever that had never been controlled in the past except in a very unsatisfactory manner, quantitatively speaking. From Naples there went to remote areas of Italy individuals who had been exposed. Two individuals, refugees from Naples, developed typhus fever in that area. Minute men were sent out from the Department of Preventive Medicine of the Mediterranean Theatre to delouse the entire native population in those two villages. There were no secondary cases from the primary subjects. There was a grace period of ten days before lice, biting the individuals suffering from typhus fever, could in turn transmit to second susceptible human hosts.

After attention to the control of vectors and reservoirs of Rickettsiae, the measures of protection of exposed susceptible human beings are natural objectives. Vaccination by the attenuated Dermacentroxenus rickettsi gives some protection against Rocky Mountain spotted fever. If such a person incurs the disease, its course is much less severe. Vaccination has been proposed for all rickettsial diseases. In World War II, it was the prophylactic procedure in military areas against epidemic typhus fever, particularly. According to the figures available to us now, there were less than ten vaccinated American soldiers who developed typhus fever in the European Theatre. Clinical observation of several of these patients indicated a marked amelioration of ordinary severity. Even though one was a rather senior major, and ordinarily individuals who are past forty have a severe expression of the disease, he had a very mild course, with no cerebral manifestations and no evidence of renal involvement. Vaccination affords a definite degree of protection; and if the barrier be crossed by overwhelming infection, the clinical course is not a severe one. The most recent development is chemoprophylaxis. Smadel and his fellows, studying scrub typhus fever in Malaya, have indicated that in this particular infec-

tion (Rickettsia tsutsugamushi) there is protection but rather of a suppressive order. The analogy to the use of atabrine in malaria is entirely proper. The chemoprophylaxis must be carried on with Chloromycetin®, or chloramphenicol for a continued period after exposure to insure that the resistance of the host will be built up sufficiently to resist the infection which has been sustained whether or not killed at the moment.

The actual treatment of the rickettsial disease imposes the closest general care and nursing. The mortality of epidemic typhus fever, which is ordinarily 20 to 25 per cent, can be reduced to 10 per cent by proper nursing, good nutrition and hydration. The experiences with convalescent serum and hyperimmune serum in therapy have not been particularly gratifying or promising. The availability of paraaminobenzoic acid came to us late in the World War II period and unquestionably, had there been nothing better, it would be the treatment of choice today. Twenty to 30 milligrams per cent was the objective for typhus fever; 40 to 60 milligrams per cent in the blood for the patient with Rocky Mountain spotted fever. There have come into our hands two different agents in recent years. They are chloramphenicol (Chloromycetin®) and aureomycin, both of which are effective against the Rickettsiae. Aureomycin is used in doses that involve first a loading procedure, an initial dose of 30 to 40 mg. per kilogram. This amounts to between 2 and 4 grams for the first dose and then ½ gram three to four to six times a day, depending upon the severity. In the case of chloramphenicol (Chloromycetin®), it ranges from 50 to 75 mg. per kilogram; and after this loading dose, the dosage is ½ gram four to six times a day, or a total of 2 to 3 grams of the chloramphenicol daily. By the use of either of these two measures, antibiotics, aureomycin and chloramphenicol, we may expect to see the control of toxic manifestations, alleviation of constitutional symptoms, with a drop of the temperature to normal in thirty-six to forty-eight hours The prospect of prompt cure of rickettsial diseases is unusually bright in the light of these newer antibiotics.

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In summary, historically the most important of the rickettsial diseases is epidemic typhus fever. Only strict hygienic measures can avoid its spread from areas of endemicity in this day of speeded transportation. Indeed, the barrier has already been breached in the fact that in New York City recurrently, lately in Boston and most recently in Philadelphia, instances of Brill's disease have been reported. Endemic typhus fever is with us always in the Southwest and in the Southeastern states. Travelers in these areas and to Mexico periodically return to our removed communities with endemic typhus fever. A few years past, Q fever was deemed a native of Australia. World War II witnessed its appearance in the Mediterranean Area, and now there have been three epidemics in the United States, and there is knowledge of the infected milk shed of the Los Angeles district. Two new rickettsial diseases, Bullis fever and rickettsialpox, have been reported in the United States in the past four years.

Gentlemen, as physicians, as clinicians, in daily contact with illness attended by vague general manifestations, certain cutaneous eruptions, and classical laboratory findings, I charge you with the responsibility of staying diagnostically awake to the rickettsial threat.

PRESIDENT DEWIS—Thank you very much, Dr. Middleton. That was most interesting. I think perhaps some of our members might like to ask Dr. Middleton some questions and I am sure he will be very pleased to answer any questions.

DR. D. SERGEANT PEPPER—I am interested in the transmission of the Q fever. I do not think we have any bandicoots in this country. I wonder what the animal is, and I should also like to know whether it is possible that the Rickettsia can be passed from the milk of these animals in the Western states directly to the patient, or is it just a chance finding in the milk that shows infection of the animals?

DR. MIDDLETON—Dr. Pepper's questions are both very pointed. In the first instance, we have said that there was this natural history, the tick to the bandicoot, to the tick, to the bandicoot, to the tick, with man and cow as possible dead-end victims.

There has been no proof of tick bite in any of the reported epidemics in this country. There has been the suspicion that the tick has infected the cattle, or that the feces, which are the infected portion from the gastrointestinal tract of the arthropod vector, are deposited on the hide of the cow, the sheep, or the goat, and likewise in the blood and in the intestinal contents. The dust from the infected animal containing the Rickettsiae, by insufflation rather than through cutaneous breaks, gains access to the body of the susceptible host. This mechanism in all probability is responsible for the epidemics in this country, and this is likewise believed to be true for the North African and Italian experiences.

Now, turning to the question of the possible significance of these surveys of the milk shed of Los Angeles County, it is my firm conviction that when surveys are made elsewhere, they will demonstrate the existence of other foci but perhaps not so high incidence of Rickettsia burneti as they have there. There is no present information as to the impact of this particular infestation in that local area upon the incidence of Q fever. Currently it is not believed to be a factor; but looking ahead from the public health standpoint I believe we must be prepared, and first of all prepared to recognize the condition when it does occur. Currently it may be assumed simply a fortuitous circumstance that it has been discovered in Los Angeles County because of the survey. Actually, from a practical standpoint, we must look forward to what may be the total impress of that disease incidence.

Dr. Donald E. Yochem—In this present day of so many antibiotics from which to choose in the treatment of the various diseases, is it not true that it would be wiser at this time, according to the reports, to use aureomycin exclusively in treating rickettsial diseases?

Dr. Middleton—The implied point in Dr. Yochem's question is that of rickettsial resistance, if not bacterial resistance, that may develop.

From the standpoint of Smadel's experience in Malaya, there is no development of resistance by Rickettsia generally

to chloramphenicol or aureomycin. If we are looking to the application of one or the other of these agents in bacterial diseases at a later time, Dr. Yochem may have a point. From a practical standpoint, those of you who have had the opportunity to use aureomycin and chloramphenicol will agree that because of the gastrointestinal discomfort—cramps, nausea, and diarrhea—that attend the use of aureomycin, chloramphenicol is the drug of choice.

There is not enough differential from the range of trends for dosage, loading and continuing between these two agents to warrant a preference. A background of experience must eventually answer the questions raised, authoritatively and finally. From the evidence at hand, there is no development of resistance on the part of the Rickettsia resulting from the administration of aureomycin and chloramphenicol experimentally or clinically.

DR. JOHN D. CHAPMAN—I should like to ask Dr. Middleton if he can tell us why there was such a great discrepancy in the mortality figures between the Snake River Valley and the Bitter Root.

DR. MIDDLETON—We know no more than the Indians knew back in the pre-white-man days.

DR. B. L. HUNTINGTON—I should like to ask what evidence there is that we are to expect late complications in people who have had scrub typhus fever.

DR. MIDDLETON—That question can be answered only in theory. The incidence of myocardial injury was high. The mortality of 9 per cent was practically entirely on the basis of myocardial damage. The fact that these rickettsial diseases affect widely the arterioles in the process of vasculitis is not presumptive evidence but is a leading detail that should not be overlooked when we are following the ultimate course of these patients.

Frankly, there is nothing to support my doubt, but it is simply one of those questions that has been raised.

DR. RICHARD E. NICHOLSON—Is there remission of symptoms if these drugs are given?

DR. MIDDLETON—Yes, in my own experience—then continue for a week after the temperature has been normal.

DR. NICHOLSON—Do remissions occur very frequently?

DR. MIDDLETON—Relapses occur if the drugs are discontinued immediately upon the subsidence of temperature to normal, and that is a very important matter. I am glad it was brought up in this relation, because the inclination is to stop therapy too soon. In our experience, it is much safer to carry on for a week of afebrile course before discontinuing antibiotics in the rickettsial diseases.

DR. BERTHOLD R. COMEAU—You have not mentioned the use of heparin and dicumarol. Because of the vasculitis noted, would that not be good treatment?

DR. MIDDLETON—We have not used either heparin or dicumarol. There are hemorrhages as well as thromboses, and the propriety of giving anticoagulants is a serious question in my mind. Dicumarol has been suggested and used, but I believe that in a large series of patients the danger from hemorrhage because of depleted prothrombin would be greater than any advantage that might accrue to its use. Theoretically I would not use it. Practically I have not used an anticoagulant.

PRESIDENT DEWIS—Well, Doctor, it appears as though you have answered all the questions. Thank you very much, sir, and it has been very kind of you.

Our next paper is entitled "Some of the Causes of Low Back Pain," by Dr. Alan DeForest Smith. Dr. Smith is Professor of Orthopedic Surgery at the College of Physicians and Surgeons of Columbia University, Surgeon-in-Chief of the New York Orthopedic Dispensary and Hospital, and Consulting Orthopedic Surgeon to Roosevelt Hospital in New York. He is a Fellow of the American Academy of Orthopedic Surgeons, and a member of numerous organizations associated with his specialty. He has had a special interest in military and traumatic surgery, and has contributed extensively to the literature on many orthopedic subjects, including that on our program today. It is a pleasure to present Dr. Smith.

# SOME OF THE CAUSES OF LOW BACK PAIN

ALAN DEFOREST SMITH, M. D.
*Professor of Orthopedic Surgery*
*Columbia University College of Physicians and Surgeons,*
*New York*

The frequency of pain and disability in the lumbosacral region indicates that this is a vulnerable point in our anatomy and suggests the presence of some mechanical fault or weakness. This assumption is confirmed by a study of the anatomy of the past. Probably the most important single factor in producing this weakness is the change in mechanics resulting from man's assumption of the upright posture. Although this must have occurred untold ages ago, he has not adapted himself to the marked change in the forces which this new posture produced. As Splithoff aptly phrased it, "When man assumed the upright posture he not only set himself apart from the animal kingdom, but he also set the stage for a series of disorders of the low back which have plagued him since".

The lumbosacral joint is the junction of the free moveable portion of the spine with the fixed portion or sacrum. It also is the transition point between two curves, the forward lumbar and the posterior sacral curve. Both of these facts render it a comparatively weak point mechanically.

In addition to the general alteration of mechanics which this has involved there are a number of apparently minor variations in the anatomy of the lumbosacral joints which at first sight seem trivial but which on further study prove to be of some importance in their effect upon the ability of the joints to meet the strains imposed upon them. One of these is the variation in the so-called lumbosacral angle. The lumbosacral angle is that subtended by the plane of the upper surface of the sacrum and the horizontal. The more nearly

vertical the upper surface of the sacrum, the platform upon which the fifth lumbar vertebra rests, the greater is the shearing strain which tends to force the fifth lumbar vertebra downward and forward. In the case of an otherwise normal lumbosacral joint the spine cannot actually become displaced, but nevertheless the greater this force, the greater is the strain which is placed upon the ligaments and the intervertebral disc. The average lumbosacral angle is about 42 degrees but it may approach 90 degrees in some individuals.

The lateral articulations between the fifth lumbar vertebra and sacrum which are situated at the ends of the laminae on each side are, in themselves, of a good deal of importance. They lock the vertebra in place and determine in large degree the magnitude as well as the direction of motion in the joint. These facets usually are concavo-convex or cup shaped and the plane of each joint is oblique or intermediary between the sagittal and coronal planes of the body. This, however, is subject to the widest variation. Both joints may face forward and backward, as do those in the dorsal vertebrae, or both may face inward and outward. Furthermore one may be sagittal and the other coronal. In the last instance and when both joints face forward and backward, or as the anatomists say, are coronal, the lumbosacral joint is much more unstable.

Usually there is no appreciable backward or forward movement of one lumbar vertebra upon another, but in some individuals there does occur a backward displacement or retroposition of the fifth lumbar vertebra upon the sacrum, or more rarely of one of the higher lumbar vertebrae upon the one below. This may be evident in an x-ray taken with the subject lying down or may be present only when he is standing. It usually becomes more marked in the standing position. This displacement usually is not marked, amounting only to a fraction of an inch, but when present in any demonstrable degree it is an indication of a weak, unstable joint. It occurs practically always only in the presence of antero-posterior or asymmetric lateral articulations and thus appears to be a consequence of that condition. Individuals in whom this dis-

placement occurs have potentially weak backs and are subject to repeated occurrences of pain not infrequently associated with sciatica.

The opposite, or forward displacement of the fifth and much less often of the other lumbar vertebrae, also is found. It is called spondylolisthesis and first was noticed and described by the obstetricians, because when pronounced it is an obstacle to normal labor. Its importance to the orthopedist lies in the fact that it also renders the back weak and unstable and in many, though not in all instances, gives rise to clinical symptoms. Studies of large numbers of x-rays and skeletons indicate that the defect from which it arises is present in about 5 per cent of individuals. This defect is a failure of ossification in a small area of the lamina on each side, the so-called pars intermedia, lying between the upper and lower articular processes. The posterior arch of the vertebra then is connected with the pedicles and body only by fibrous tissue which may stretch as a result of the great strain imposed upon it, permitting the body to move forward. In some cases the defect exists without any displacement of the vertebra but even this condition means a weak back, vulnerable to strain. In others the displacement varies from slight to the entire width of the vertebral body, which in some cases goes forward and downward into the pelvis. In addition to backache, the stretching of the lumbosacral nerves may cause sciatica. The condition undoubtedly is congenital and sometimes may be hereditary.

Another quite common occurrence is that of marked enlargement of the transverse process of the last lumbar vertebra on one or both sides, which takes on the form and shape of the lateral mass of the sacrum and makes contact with the sacrum. These are called numerical variations because their effect is either to reduce or increase the number of lumbar vertebrae. The average human has 24 free and separate vertebrae, 7 cervical, 12 dorsal and 5 lumbar. The 25th and succeeding vertebrae join together to form the sacrum and coccyx. Some individuals, however, have only 23 separate vertebrae. The 24th, ordinarily the 5th lumbar, has joined the sacrum. Still

others have 25 free vertebrae, the 25th having retained its freedom and become in all respects a true member of the lumbar group. The meaning of these numerical variations is that an evolutionary process is going on in the human spine with a tendency for the pelvis to migrate upward and include the last lumbar vertebra in the sacrum. This has a mechanical advantage in an animal who is habitually upright, in that the shorter the spine the more easily is it supported and the less strain is there upon it. Viewed in this light persons with only four lumbar vertebrae represent an advance in the evolutionary process and those with 6 an arrest. It is interesting to find that the anthropoid apes, who are making an attempt to stand erect, but have not succeeded to the extent of their cousin, homo sapiens, also exhibit these variations in the number of free and fixed vertebrae.

When the variation is complete, either an advance or arrest, and the vertebra involved is completely joined to or completely free from the sacrum, the result is that those with the shorter spine have a relatively stronger and those with a longer spine a relatively weaker low back. There are numerous instances, however, in which the process is incomplete and asymmetric. One side of the last lumbar vertebra may make contact with but not be solidly fused to the sacrum and the other side may have all the characteristics of a normal lumbar vertebra including a lateral articulation. This causes a marked difference in degree of movement and of stability on the two sides and such cases are potential victims of low back disorders.

It should be emphasized that these anatomical variations just described are not necessarily causes of low back pain, but that singly or in combination they represent a structural weakness which renders the person having them more vulnerable to the effects of strain which occurs even in normal activities, in great degree in this region. When they are found in one who has a long history of repeated or continued low back pain they are significant.

Another structure in this region which is of great importance in the question which we are discussing is the inter-

vertebral disc, and particularly the last two discs between the fourth and fifth lumbar vertebrae and sacrum. It may not be amiss to review briefly the salient features of its makeup. The disc consists, you will remember, of concentric rings of tough fibro-cartilage called the annulus fibrosis. In the center of this structure is a space which contains a soft fibrous, but semifluid mass of tissue, called the nucleus pulposus. It is the modified vestige of the primitive notochord. As one advances in age the nucleus loses some of the liquid component and degenerates into a tough fibrous mass. During the greater part of life, however, it remains practically a liquid ball and conforms to the laws of hydraulics. That is, under stress its shape may alter but it is not capable of being compressed. At the upper and lower surfaces of each disc is a plate of hyaline cartilage which acts as a top and bottom for the disc and which is firmly attached to the adjacent vertebra. The periphery of the disc is attached to the longitudinal ligaments which join the vertebral bodies. In addition to joining the vertebrae together the discs act as shock absorbers, taking up some of the longitudinal strains upon the spine and each nucleus pulposus serves as a liquid ball bearing through which pass the axes of motion of one vertebra upon another.

Thus if an intervertebral disc becomes narrowed and its nucleus becomes small or disappears, as frequently happens at the lumbosacral junction as a degenerative process in older individuals, or less frequently from severe trauma or disease, the mechanics of this joint are adversely affected. The axis of motion no longer occurs through the center of the disc but is transferred backward to structures which are not adapted to receive it. Movements therefore become limited and often painful. Furthermore, when the two vertebrae become approximated as a result of the thinning of the disc, the intervertebral foramina through which the nerve roots pass become much smaller. Normally there is ample latitude between the size of the foramen and of the nerve root to allow for considerable variations in the size of the former resulting from spinal movements. The last intervertebral foramen, however, is the smallest in the lumbar area, and the nerve

root is the largest. Therefore when this nerve exit is contracted it may result in actual pressure upon the root and cause radiculitis.

This much has been known about the disc for a long time. More recently another phenomenon relating to it has been described constituting one of the most important contributions to the subject of low back pain that ever has been made. That is that the annulus or peripheral part of the disc may rupture permitting the soft central nucleus to be extruded or herniated. The disc is least well supported by ligaments postero-laterally on each side and it is at this point that the herniation takes place in the great majority of instances. There are other cases in which the cartilage plate on the top or bottom of the disc may break or perforate and the nucleus material may be forced into the cancellous substance of the vertebral body, but this is not fraught with the consequences of the postero-lateral herniation and has not nearly as much practical importance.

The credit for describing herniation of the nucleus pulposus and discovering its frequency and clinical importance belongs to Mixter and Barr of Boston. As in most discoveries, however, others before them described the condition but failed to grasp its real importance. Among them are Goldthwait, Stooky and Schmorl, the German pathologist.

Rupture of the annulus and protrusion of the disc may happen suddenly in a normal disc as the result of a sudden great pressure such as results from a heavy lifting strain or a fall, or it may occur gradually in a disc which has become weakened by degenerative changes and in which little more than the usual everyday strain is necessary to precipitate the final occurrence. The great majority (more than 95 per cent) of ruptures occur either in the disc between the fifth lumbar and sacrum or in that between the fourth and fifth lumbar, probably because, for reasons previously described, the strain is greater in this area. More rarely herniation may be found higher in the lumbar, or in the lower cervical area.

Unfortunately the point at which the disc usually protrudes is precisely that where a nerve root lies in contact with it on its way to leave the spinal canal to join the lumbosacral plexus and form the sciatic nerve. Pressure on the nerve root from the protruding disc results in pain which is referred along the course of the sciatic nerve. Thus, sciatica, or pain along the back or side of the thigh and the outer side of the leg, is the commonest symptom of a herniated disc. In some cases, however, and especially in the early stages, the pain may be confined to the low back on one side, extending later into the lower extremity. The pain often is accompanied by a sensation of numbness, or pins and needles, and is accentuated by coughing or straining, which raises the pressure of the spinal fluid.

As the nerve root passes over the intervertebral disc, which lies in front of it, the ligamentum flavum is directly behind it. This strong fibroelastic ligament connecting the two adjacent laminae often is very thick, and in such cases may add to the pressure of a protruding nucleus upon the root.

In addition to sciatica, numbness and weakness in a lower extremity, certain physical signs tend to confirm the diagnosis of nerve root pressure. The most important are:

1. Limitation of flexion of the hip with the knee extended, or so-called straight leg raising. This is accompanied by pain in the back and leg.

2. Diminution of sensation on the outer side of the leg and lateral, dorsal or inner aspect of the foot, depending upon the nerve root involved.

3. Diminution or suppression of the ankle jerk.

4. Atrophy of the muscles of the leg and thigh.

5. Weakness of the muscles of the leg.

6. A list of the trunk away from the side of the pain.

Any or all of these signs may be present. That most frequently found is limited straight leg raising. On the other hand, all of these signs may be lacking in the presence of a

real herniation. How then is a diagnosis to be made? An ordinary x-ray of course will not reveal any alteration in cartilaginous or soft tissues. It may show that a disc is thin but this by no means proves that there is a nucleus herniation. In the average case the history together with a group of typical physical signs is sufficient to make the presumptive diagnosis so strong that an exploration of the two lower discs on the side of the pain is justifiable.

In cases of only a few weeks' duration, it is best to keep the patient at rest and under sedation to see whether the pain does not cease spontaneously before resorting to operation. In doubtful cases it may be necessary to resort to a myelogram, which is an x-ray taken with an opaque substance such as "Pantopaque" in the spinal canal. A few cc. introduced in the lower lumbar canal will often outline a herniation exactly. This procedure is by no means infallible, however, and should be done by one experienced in its technic and interpretation. There are too many false negatives and positives for us to rely upon it entirely and it should not be necessary to resort to it as a routine. It usually is possible to withdraw most of the "Pantopaque" after the test but that which does remain is absorbed very slowly, if at all, and sometimes gives rise to unpleasant sequelae.

It is well to remember that by no means all cases of sciatica are due to a ruptured disc. One serious, but fortunately infrequent, cause is a spinal cord tumor. Tumors of the vertebrae or sacrum, arthritis, anatomical anomalies of the vertebrae, such as transitional lumbosacral vertebrae, spondylolisthesis, and posterior displacement of the last lumbar vertebra, and simple thinning of a disc without herniation are among the many causes which may give rise to this symptom.

As with any new discovery we were inclined at first to be carried away by this new concept and to exaggerate its frequence and importance. As our knowledge of the condition has increased we have been able to evaluate it more accurately and to assess more correctly its true place among the causes of back pain. It still remains one of the most important.

Time will permit no more than a very brief mention of the treatment of low back pain. In the great majority of cases, due to causes other than herniation of a nucleus, conservative measures such as rest, physical therapy and supports suffice. In a small number of patients with persistent backache which does not yield to such treatment, and especially those with some definite structural weakness, a lumbosacral spine fusion is advisable. At the New York Orthopaedic Hospital, where this operation originated, we find that we operate on only from 5 to 10 per cent of all patients with back pain.

A herniated nucleus pulposus which does not yield within a reasonable time to rest, should be operated on. Removal of the herniated cartilage in the great majority of cases gives prompt and complete relief. The failures usually are due to a mistake in diagnosis.

A question which has been debated extensively in the past few years and which still has not been settled to everyone's satisfaction is whether a spine fusion should be done when a herniated nucleus is removed. Those of us who have advocated doing so believe that we get the best results by doing the combined operation. It is our contention that frequently a disc ruptures because it has been subjected to an undue amount of strain caused by a weak, unstable joint. Naturally this strain will continue after excision of the nucleus and is likely to cause backache if not sciatica. Also, degeneration of the disc after removal of the nucleus is apt to cause the train of events which was described in the earlier discussion of the disturbances of the function of that structure. In many instances patients who have been relieved of their sciatica by the disc operation, return later complaining of a weak painful back, which might have been avoided by a spine fusion. Dr. Joseph Barr, who with Mixter, wrote the original paper on the disc, recently announced that a series of cases with the combined operation did better than others that had removal of the herniation alone. That has been my experience, also.

The technic of removing a herniated nucleus has now been perfected and simplified so that it no longer is the formidable procedure that it once was; and it necessitates the removal of

very little of the laminae. Usually the combined operation can be done within a reasonable time. Recent improvements in the spine fusion operation itself, which include internal fixation with screws, often make it possible to get the patient out of bed in two weeks and out of the hospital in three, which is little if at all longer than the time required for the operation on the disc alone.

It may seem unusual that in a discussion of this subject I have failed to mention the sacroiliac joints, which are blamed so frequently for low back pain. Goldthwait thought at one time that the sacroiliac joints were the cause of a great many of these conditions and his influence had much to do with the frequency of this diagnosis. He later changed his opinion and now thinks that the lumbosacral joint nearly always is responsible. The ligaments of the sacroiliac joints are among the strongest in the body. It rarely is possible to demonstrate any subluxation in these joints by x-ray, and in cases where there is a recognizable derangement there often is no pain. For these reasons it is believed that low back pain rarely is due to sacroiliac strain.

PRESIDENT DEWIS—Thank you very much, Dr. Smith. I am sure our members have a few questions they would like to ask you, and perhaps you would like to answer them.

DR. J. GILBERT FALCONER—In this mechanical condition, what apparently happens in an apparently authenticated case which does improve with straight rest in bed, and why does the patient improve?

DR. SMITH—One of the interesting features of this condition is the fact that it often is intermittent, that is, characterized by complete remissions, and sometimes these last for a long time. One can only speculate about that. I suppose that the most probable explanation is that the herniation is partly reduced or goes back again. It may be that something has produced unusual strain or pressure on the nerve and caused it to become acutely painful and then it comes back to its former position. The fact that pain completely disappears does not mean it necessarily will last. That individual may

show up again with a recurrence of pain. However, after the first attack, or during the first attack, if relief is obtained by rest I think that is the thing to do and later deal with it surgically only if it recurs.

DR. JOSEPH C. HORAN—As I understood it, Dr. Smith, the cause of the herniation is very often trauma but may not always be trauma. Is there any way to tell which is which and what the percentages are?

DR. SMITH—No, I do not think so. If the attack of pain comes on immediately after some competent injury, I think the injury should be given credit for the cause of the pain, but in many cases there is no history of injury at all that the patient can remember. It is difficult for him to recall any injury, especially if it was rather trivial, such as lifting an object, tripping, stumbling, or falling. Each individual case must be evaluated on the history, severity of the trauma, and how soon afterwards the pain appeared.

DR. HORAN—Are there any cases that are not traumatic?

DR. SMITH—Yes, I think there are. In a good many cases in the middle-aged and older individuals who have disc degeneration, a very common occurrence in the lumbosacral region, a slight amount of extra strain which one gets every day may cause it finally to rupture.

PRESIDENT DEWIS—There must be more questions you would like to ask while we have Dr. Smith up here.

DR. PEPPER—Have you noticed any association of night cramps with intervertebral discs?

DR. SMITH—These people do have night pains and cramps sometimes, but I have not noticed them especially in disc cases. Their occurrence might be due to the posture of the patient in sleeping.

PRESIDENT DEWIS—Thank you very much.

I think we are particularly honored this afternoon, for the first paper on the program "Voluntary Health Insurance, Its Successes and Its Failures to Date," will be given by Dr.

Paul R. Hawley, Chief Executive Officer of the Blue Cross and Blue Shield Commissions. Dr. Hawley, or General Hawley, as he is more commonly known, served for thirty years in the Medical Corps of the United States Army. He was Chief Surgeon of the European Theatre of Operations during World War II and was the recipient of many decorations from the United States and allied countries. Before assuming his present duties, he was Chief Medical Director of the Veterans Administration from 1945 to 1947. We are all very glad, I am sure, to welcome Dr. Hawley.

# VOLUNTARY HEALTH INSURANCE
# ITS SUCCESSES AND ITS FAILURES TO DATE

PAUL R. HAWLEY, M. D.
*Chief Executive Officer*
*Blue Cross and Blue Shield Commissions, Chicago, Illinois*

The successes of voluntary health insurance must be measured both in terms of how much it has reduced the burden of the costs of medical care, and how much it has contributed to the preservation and the extension of the system of medical care which has made American medicine of the 20th Century the finest in the entire history of the art. It is not necessary to emphasize to this audience that voluntary health insurance has not reduced, and cannot reduce, the cost of medical care; but such a misstatement is made occasionally and it is one that should be corrected at every opportunity. Voluntary health insurance has, however, gone a long way toward easing the burden of this cost, even though it still has a long way to go before it can boast of a task fully accomplished.

The interests of the people and the interests of the institutions providing medical care for the people are closely bound together, even though there may be small conflicts of interest upon occasion. It is distinctly in the interest of the people that the agencies providing medical care be stimulated toward expansion and improvement. For this reason, it is most important that voluntary health insurance contribute to this end rather than assume the exclusive position of a bargaining agent for the consumer of medical care in a battle to lower costs. This is not to say that voluntary health insurance should pay one penny more for the medical care of its subscribers or policyholders than this care is worth; but neither is it to say that it should endeavor to obtain this care at a figure that will impair the usefulness of hospitals through adding to deficits.

There is another reason why the health insurance industry must interest itself in the producers as well as the consumers of medical care. Insurance is one of the important bastions of free enterprise in this country—and one of the few which is now under attack by those who would socialize America. Voluntary hospitals and an unregimented medical profession are parts of the free enterprise system which must be protected. The economic security of doctors is not as yet threatened; but that of voluntary hospitals is in a precarious position. If voluntary hospitals are unable to survive in a free enterprise system, the government must, in the public interest, support them; and government support means government control. Once the hospitals succumb, the medical profession will fall shortly, and we shall have the complete socialization of medical care.

As regards the number of people who are protected by voluntary health insurance, the most conservative estimates are that more than 60 million of our citizens are protected to some degree against the cost of medical care. Of these, about 35 million are enrolled in Blue Cross. In addition to some 12 million Blue Shield subscribers who are also enrolled in Blue Cross, there are about one million who carry Blue Shield alone. This makes about 36 million different individuals who are enrolled in the voluntary nonprofit plans. Some 25 million additional people either carry commercial health insurance, are enrolled in local cooperatives or are protected by employee benefit associations.

In this year of 1949, Blue Cross will pay approximately 300 million dollars to hospitals for the care of Blue Cross subscribers. This will represent between 80 and 85 per cent of their total hospital bills.

Blue Shield will pay approximately 100 million dollars for the medical care of its 13 million subscribers. Dr. Frank Dickinson, the economist of the American Medical Association, estimates that this represents about 55 per cent of the total medical bill of Blue Shield subscribers, although it is practically all for medical care in hospital since few Blue Shield Plans cover home and office medical care.

This introduces the question as to how much protection against the costs of medical care is justifiable on economic grounds. Approximately one-half the total annual medical bill of the country is for hospitalized illness. This one-half of the total bill is borne by 10 per cent of the population. The other half is spread among 90 per cent of the population.

Obviously the small spread of the cost of hospitalized illness makes this part of the health bill a proper item for insurance. Through insurance this half of the bill can be spread over ten times the number of people as would have to pay it were they not insured. In this manner, the cost of hospitalized illness to the individual family can be reduced to a sum well within the budget of almost all self-supporting people. The cost of such protection for an entire family will not exceed $75.00 per year, which is approximately the cost of one package of cigarettes a day. There are few family budgets that will suffer from such a charge, especially when payments are made monthly.

But what about insuring the other half of the medical care bill—that half that is paid for medical care outside of hospitals? In the instances in which Blue Shield Plans have experimented in covering home and office visits, it has been found that more than 50 per cent of these casual medical bills are for sums less than $6.00, and that the administrative cost of processing and settling such a claim is around $3.00 per claim. This means that the insured person, in the aggregate, is paying at least 50 per cent more, and often twice as much, as the service is worth. Thus we see that we encounter the law of diminishing returns when we attempt to insure against the costs of small medical bills. The same situation will obtain in government compulsory insurance, thus greatly increasing the cost of medical care—a fact that is not often recognized.

Efforts to lessen the administrative cost of such protection will only increase it. For example, a policy which includes a deductible clause will necessitate a great amount of paper work on the part of physicians and the insured person—certified copies of all medical bills paid during the period by the

insured person so that the amount of reimbursement he is entitled to, after deduction, can be determined.

For these reasons, I am firmly of the opinion that, *at the present time at least*, it is neither feasible nor economical to extend the scope of protection much beyond the cost of hospitalized illness. It is also probable that full protection would lead to abuses of the service by some people, and this would raise the cost of the protection.

In this connection, you must remember that health insurance is the only kind of insurance that is not protected by law against abuses. Even the indemnity type of health insurance is protected to some degree by a dollar limitation upon benefits; but service plans are entirely at the mercy of the patient, the physician and the hospital. You are all aware of the impossibility of operating fire insurance without strict laws against arson; and I suppose that, to some degree at least, life insurance is protected by laws against murder. Marine insurance, burglary insurance, bank insurance are all protected by the fact that barratry, theft and embezzlement are crimes; but a law to make unnecessary visits to a doctor a crime would obviously be impossible. So, the element of good faith, particularly upon the part of the doctor, is the only protection afforded health insurance. This element is adequate in the case of illnesses of a more serious nature—especially those requiring hospital care—but it is an element beyond the control even of the doctor in the casual visit of the patient to his office.

In evaluating the successes of voluntary health insurance, we must remember that this is a relatively new field of insurance, that it had to start with absolutely no actuarial experience, and that, even now, actuarial data are not wholly adequate. The rapidly rising costs of health care have been no special problem to the plans which offer only indemnity benefits, but they have been a source of great difficulty to the service plans. With both hospital costs and utilization rising in the past five years, service plans have been forced into frequent raises in rates. Such raises have not endeared them to their

subcribers, although cancellations of enrollment for this reason have been astonishingly few.

I think we may summarize the successes of voluntary health insurance as—

a. A convincing demonstration that burdensome medical costs are insurable at a rate within the reach of almost all self-supporting people.

b. A steady and healthy growth of voluntary plans until now at least 40 per cent of our total population, and perhaps 50 per cent of our insurable population, are protected to some degree against the costs of health care.

c. The provision of assured revenues to hospitals which offset, to some degree, the diminishing returns from endowments and replace the sources of private philanthropy which have largely been dried up by heavy taxation.

d. A reduction in medical indigency which both has decreased the amount of charity work required of voluntary hospitals and has increased the self-respect of many families with marginal incomes.

So much for the successes. In my opinion, the failures are of far greater importance, especially at this time. First among these failures, I would list the failure to educate people that health insurance has become a necessity in perhaps 80 per cent of the families in this country. Since the need for medical care crops up at irregular and unpredictable times, too few people even consider it in the preparation of the family budget. Furthermore, since both the amount of medical care required, and its cost, are as equally unpredictable as the date, it is impossible to budget for it upon a pay-as-you-go principle.

So, people must first be educated to the fact that medical care is just as much a necessity as food, shelter and clothing; and, second, that its cost can be budgeted, but only in the form of insurance. While there is a slowly increasing realization of these facts, we have not moved fast enough in this direction.

Second, we have not convinced enough people that voluntary health insurance is to be preferred to compulsory health insurance. Too many people, already convinced of the necessity for health insurance of some kind, either express a preference for, or appear to be willing to accept, compulsory health insurance.

There are several reasons for this failure, the principal one, in my opinion, being the strict enrollment or underwriting policies which have been followed until the present by almost all commercial carriers and by too many Blue Cross and Blue Shield Plans. Group enrollment has been the rule, and nongroup enrollment the exception. One cannot be too critical of such a policy. The dangers of adverse selection in nongroup enrollment are real and cannot be discounted, as a few plans have discovered to their sorrow. Commercial carriers must show profits, whether they be stock or mutual companies; and the nonprofit plans usually operate upon such a small margin that they dare not load up on poor risks.

Then, again, the potential has been huge. Why search the countryside for the occasional tree when there were thick forests ready for the axe? Both acquisition costs and losses are less in large groups; and, so long as there were large groups still untouched, few plans bothered much about small groups and individuals.

The time is past when individuals can be ignored in voluntary health insurance. The most important of the self-employed, from our point of view, are the farmers. The factor of adverse selection, a real danger in the beginning of nongroup enrollment, diminishes in importance as each per cent of the population is added to the enrollment. Even at the outset, it can be controlled by various devices, such as community enrollment drives and restricted periods during which individual enrollment is accepted.

The next failure, which I would list, is one almost entirely limited to the nonprofit plans. This is the failure to offer more than one type of contract. There is always, of course, the group with very low incomes who can afford only the

lowest possible cost of protection—as, for example, ward accommodations on a full service basis. This is by far the most important group to be protected, and an offering to them must never be priced out of the market.

However, they are not the only group that needs and wants protection. There are many people, higher in the income scale, who can afford and who want somewhat more elaborate accommodations.

Finally, people vary with respect to the proportion of the risk they want to carry themselves and the proportion they want to insure. This is true in all fields of insurance. Perhaps there is no greater difference of opinion upon this point than in the field of collision insurance for automobiles. Some owners want complete coverage down to the last bolt or screw to be replaced. Others want protection against only serious accidents to their cars. Still others prefer to carry all this risk themselves, and to insure only against personal liability and property damage.

I am convinced that each Blue Cross Plan should offer a complete service contract, with no exclusions, to cover up to, say, 70 days of hospital care for each admission. I do not say that the sale of such a contract should be pushed; but I do think it should be made available, if only for the purpose of obtaining some accurate data on the costs of complete hospital care.

PRESIDENT DEWIS—Thank you very much, General Hawley. I believe our members might have a few questions that they would like to ask you.

DR. DAVID HALBERSLEBEN—Does the Blue Cross coverage extend over all ages?

DR. HAWLEY—Most Blue Cross plans, though by no means all, have an age limitation of around sixty-five for the original Blue Cross enrollment. But the principle is: once a Blue Cross subscriber, always a Blue Cross subscriber, and they carry their members on regardless of advancing age.

DR. ALBERT J. ROBINSON—I was interested in obtaining your viewpoint with respect to social legislation in such states as New Jersey and New York, and the relationship between such state legislation for voluntary health insurance and Blue Cross and Blue Shield.

DR. HAWLEY—I would think that the experience in Workmen's Compensation insurance has shown that private industry can compete very successfully with government operation so long as government operation is forced to follow the rules of private operation and be self-sustaining.

I have often thought the very best thing that could happen in this country would be to have government-operated health insurance operating on a completely self-sustaining principle and let private agencies compete with it. I think that would be a very convincing demonstration.

I am not speaking for my Commission's report or the report to the Directors when I say I would rather welcome such a thing, because there is no doubt in my mind that all private agencies could compete successfully with that type of operation. As the Hoover Commission showed, it costs the Government ten dollars in administration to buy two dollars' worth of bolts and nuts. I think we would have nothing to fear from it.

PRESIDENT DEWIS—Does anybody else want to ask the General a question? Thank you very much, General.

Gentlemen, our next paper is entitled "Survival of Patients with Cancer as a Function of Research," by Dr. Cornelius P. Rhoads, Director of the Memorial Hospital for the Treatment of Cancer and Allied Diseases in New York. Dr. Rhoads is also Director of the Sloan-Kettering Institute for Cancer Research, which is allied with Memorial Hospital, and he is Professor of Pathology at Cornell University Medical College. During the recent world war, he held the rank of Colonel in the Medical Corps of the Army of the United States and was Chief of the Medical Division of the Chemical Warfare Services with which he is still associated in a consultant capacity. The list of his fellowships and memberships in various pro-

fessional organizations is long and impressive. He has made extensive contributions to medical literature and is recognized as an authority on diet in experimental cancer, on clinical biochemistry of gastric and other malignancies, and on steroid metabolism. His long career in cancer research gives him unusual qualifications for today's presentation. It is a great pleasure to introduce Dr. Rhoads.

# SURVIVAL OF PATIENTS WITH CANCER AS A FUNCTION OF RESEARCH

C. P. RHOADS, M. D.

*Director*
*Memorial Hospital for the Treatment of*
*Cancer and Allied Diseases*
*New York, N. Y.*
*and*
***Professor of Pathology,***
***Cornell University Medical College***

In the course of Dr. Rhoads' remarks he quoted from the unpublished paper which is given in full below:

## THE PROMISE OF IMPROVED PROGNOSIS THROUGH CLINICAL RESEARCH

by

*Eleanor Macdonald, Administrative Assistant and Director of Information and Statistics at the M. D. Anderson Hospital for Cancer Research, Houston, Texas, Consultant in Statistics at Memorial Cancer Center, New York, formerly Research Statistician, Cancer Division, Connecticut State Department of Health; and Mary Macdonald, Biometrician of Memorial Cancer Center, New York.*

In the past few years, the appearance of valid incidence, survival and cure rates for cancer at both community and specialized cancer hospital levels has proved what has long been surmised, namely, that if the best methods of therapy could be adequately applied at the community level in all cases of cancer, the immediate increase in cures would result in a corresponding drop in the death rates of spectacular proportions.

In the United States today in a current year, an estimated 278,164 individuals seek relief for cancer for the first time, 879,550 individuals with a history of cancer are living in all

the categories from cure to terminal, and 229,765 individuals are living who have survived treatment for cancer for five or more years. Each year there are approximately 180,000 deaths reputedly from this cause. If today's population structure were to remain static and there were no increase in cancer, there would still be more than 5,000,000 individuals developing cancer in the United States in the next 20 years. The population is increasing in size, and advancing in age, with a consequent increase in cancer susceptibles, so this figure is too low. Low as it is recognized to be, it is equivalent to the combined populations of Massachusetts and Rhode Island, or 65 per cent of the population of New York City.

Comparison of the net five to twelve year cure rates for selected sites, for the years 1935–1942 of the specialized hospital, with those of the combined hospitals in an entire state, emphasizes the difference in prognosis according to specialized cancer therapy or to the community level therapy. There are variables which make this a relatively fair comparison, weighted in favor of the community if at all. The patients are seen first at the community level, and the earlier they are seen the better chance there is of satisfactory therapy. Many patients are referred to the cancer hospital after therapy elsewhere has been tried without result. The early cases of cancer of the breast, for example, are usually cared for at the community level. And yet, the net cure rate at the community level is 25.0 per cent; at the specialized cancer hospital level, 31.5 per cent. The difference in these rates means 2,670 cures for this one site alone in one year in the United States.

Table I gives the per cent of total cancer, the net cure rates at the community and specialized hospital levels, and translates these rates to terms of the estimated numbers of individuals involved in the United States in one year. The difference in individuals is shown. Beside this figure, the reported deaths for 1946 for the United States are shown. The sites chosen represent 42.9 per cent of total cancer and exclude skin. Some of the sites are considered highly accessible and amenable to cure, while others present a more acute and difficult problem. For all cancer at the community

## TABLE I

### CURE RATES FOR SELECTED SITES OF CANCER COMMUNITY LEVEL AND SPECIALIZED CANCER HOSPITAL LEVEL ESTIMATED NUMBERS OF INDIVIDUALS INVOLVED IN THE UNITED STATES THIS YEAR*

| SITE | PER CENT OF TOTAL CANCER | NET RESULTS PER CENT FREE OF DISEASES FOR FIVE YEARS | | IN TERMS OF ESTIMATED NUMBERS | | | DIFFERENCES | DEATHS, 1946 |
|---|---|---|---|---|---|---|---|---|
| | | | | | Net Estimated Cures | | | |
| | | Community Level | Specialized Hospital | New Cases in U. S. in 1 yr. | Community Level | Specialized Hospital | | |
| Lip | 1.7 | 58.2 | 67.0 | 4,422 | 2,573 | 2,962 | 389 | 613 |
| Other Oral Cavity Cancer | 3.0 | 13.3 | 20.6 | 6,773 | 898 | 1,392 | 494 | 3,948 |
| Extrinsic Larynx | .6 | 9.6 | 9.8 | 1,848 | 177 | 181 | 4 | 1,746 |
| Intrinsic Larynx | .5 | 23.4 | 44.2 | 1,518 | 355 | 671 | 316 | |
| Breast | 13.8 | 25.0 | 31.5 | 41,069 | 10,267 | 12,937 | 2,670 | 17,516 |
| Rectum | 5.2 | 11.5 | 15.7 | 8,587 | 987 | 1,343 | 361 | 10,037 |
| Stomach | 7.9 | 3.5 | 7.6 | 13,542 | 474 | 1,029 | 555 | 25,625 |
| Cervix | 6.0 | 24.2 | 26.5 | 15,089 | 3,651 | 3,999 | 348 | 17,205 |
| Corpus | 4.2 | 28.3 | 31.5 | 11,218 | 3,175 | 3,534 | 359 | |
| Total | 42.9 | 21.7 | 27.0 | 104,066 | 22,557 | 28,053 | 5,496 | 76,690 |

*Includes all patients seen irrespective of degree of advancement.

level, 25.4 per cent of males and 35.5 per cent of females who are treated with the disease still localized have survived more than five years. When regional metastasis has already occurred the survival rates dropped to 9.1 per cent for males and 19.1 per cent for females. The difference in the cure rates for those sites selected, at the two levels could mean a difference of 5,496 individuals in one year if the rates were applied to the United States as a whole. The cure rate at the community level for these sites was 21.7 per cent and at the specialized hospital level 27.0 per cent.

If it were possible to effect without delay the application of the best methods of therapy at the community level, without an additional improvement or discovery, there would be an increase in cures of 24.3 per cent in these sites of cancer representing 42.9 per cent of total new cases and 42.6 per cent of total reported deaths.

**TABLE II**

ESTIMATED NUMBER OF NEW PATIENTS WITH CANCER IN THE UNITED STATES IN ONE YEAR*

| Site | Male | Female | Total |
|---|---|---|---|
| **SKIN** | | | |
| Skin of the Head and Neck | 11,626 | 8,332 | 19,958 |
| Skin of Upper Extremities | 1,584 | 590 | 2,174 |
| Skin of Trunk | 1,255 | 1,443 | 2,698 |
| Skin of Lower Extremities | 462 | 721 | 1,183 |
| Skin (generalized, multiple, or location not specified) | 594 | 262 | 856 |
| Total | 15,521 | 11,348 | 26,869 |
| **SOFT PARTS** | | | |
| Soft Parts of Head and Neck | 330 | 328 | 658 |
| Soft Parts of Upper Extremities | 330 | 262 | 592 |
| Soft Parts of Trunk | 330 | 328 | 658 |
| Soft Parts of Lower Extremities | 594 | 262 | 856 |
| Soft Parts (generalized, multiple, or location not specified) | 33 | 32 | 65 |
| Total | 1,617 | 1,212 | 2,829 |

*Computed from the known incidence in Connecticut for a seven year average.

| Site | Male | Female | Total |
|---|---|---|---|
| **SKELETAL SYSTEM** | | | |
| Skull (including tumors of dental origin) | 198 | 196 | 394 |
| Spine (excluding sacrum and coccyx) | 132 | 19 | 151 |
| Bones of Upper Extremities, scapulae and clavicles | 198 | 262 | 460 |
| Bones of Thorax (ribs, sternum) | 52 | 65 | 117 |
| Pelvis (including sacrum and coccyx) | 132 | 65 | 197 |
| Bones of Lower Extremities | 264 | 393 | 657 |
| Bones of Skeleton (generalized, multiple, or location not specified) | 396 | 262 | 658 |
| Joints and Synovial Membranes | 33 | 32 | 65 |
| Total | 1,405 | 1,294 | 2,699 |
| **CENTRAL NERVOUS SYSTEM** | | | |
| Brain and Membranes | 2,774 | 2,296 | 5,070 |
| Spinal Cord and Membranes | 198 | 262 | 460 |
| Total | 2,972 | 2,558 | 5,530 |
| **UPPER RESPIRATORY AND ALIMENTARY TRACTS** | | | |
| Lip | 4,029 | 393 | 4,422 |
| Mucosa of Cheek | 264 | 131 | 395 |
| Gingiva (or gum) | 264 | 65 | 329 |
| Palate | 396 | 131 | 527 |
| Floor of the Mouth | 594 | 13 | 607 |
| Tongue | 1,981 | 328 | 2,309 |
| Tonsil | 660 | 262 | 922 |
| Nasal Cavity | 66 | 45 | 111 |
| Nasopharynx | 323 | 131 | 454 |
| Pharyngeal Wall | 528 | 65 | 593 |
| Extrinsic Larynx | 1,717 | 131 | 1,848 |
| Intrinsic Larynx | 1,453 | 65 | 1,518 |
| Paranasal Sinuses | 330 | 196 | 526 |
| Oral Mucous Membranes or Mouth Cavity (generalized, multiple, or location not specified) | 990 | 328 | 1,318 |
| Total | 13,595 | 2,284 | 15,879 |
| **MISCELLANEOUS STRUCTURES OF HEAD AND NECK** | | | |
| Eye, Orbital Cavity, and Conjunctivae | 396 | 459 | 855 |
| Mastoid Cells, middle and inner ear | 66 | 65 | 131 |
| Salivary Glands | 990 | 1,246 | 2,236 |
| Thyroid and Parathyroid | 330 | 918 | 1,248 |
| Total | 1,782 | 2,688 | 4,470 |

| Site | Male | Female | Total |
|---|---|---|---|
| **BREAST** | | | |
| Breast and Nipple | 462 | 41,069 | 41,531 |
| Total | 462 | 41,069 | 41,531 |
| **CHEST CAVITY VISCERA** | | | |
| Trachea, bronchial tree, and lung | 8,654 | 1,771 | 10,425 |
| Heart, pericardium and aorta | — | — | — |
| Esophagus | 3,369 | 852 | 4,221 |
| Mediastinum | 330 | 131 | 461 |
| Total | 12,353 | 2,754 | 15,107 |
| **ABDOMINAL CAVITY VISCERA** | | | |
| Diaphragm, peritoneum, mesentery and unclassified abdominal tumors | 726 | 852 | 1,578 |
| Stomach | 13,542 | 7,020 | 20,562 |
| Liver, gallbladder and ducts | 2,047 | 2,427 | 4,474 |
| Pancreas | 3,170 | 2,361 | 5,531 |
| Spleen | — | 65 | 65 |
| Small Intestine | 396 | 459 | 855 |
| Large Intestine—right | 3,038 | 3,739 | 6,777 |
| Large Intestine—left | 8,786 | 8,725 | 17,511 |
| Large Intestine (generalized, multiple, or location not specified) | 1,915 | 2,165 | 4,080 |
| Rectum | 8,455 | 5,642 | 14,097 |
| Anus | 132 | 131 | 263 |
| Total | 42,207 | 33,586 | 75,793 |
| **URINARY TRACT** | | | |
| Kidney | 2,312 | 1,377 | 3,689 |
| Adrenal | 132 | 656 | 788 |
| Ureter | 66 | 24 | 90 |
| Urinary Bladder | 5,879 | 2,296 | 8,175 |
| Urethra | 66 | 196 | 262 |
| Total | 8,455 | 4,549 | 13,004 |
| **GENITAL TRACT & EXTERNAL GENITALIA (MALE)** | | | |
| Prostate, seminal vesicles, and adnexa | 13,476 | — | 13,476 |
| Glans and foreskin of penis | 132 | — | 132 |
| Testis, epididymis, and spermatic cord | 1,321 | — | 1,321 |
| Total | 14,929 | | 14,929 |

| Site | Male | Female | Total |
|---|---|---|---|
| **GENITAL TRACT & EXTERNAL GENITALIA (FEMALE)** | | | |
| Corpus of Uterus | — | 11,218 | 11,218 |
| Cervix of Uterus | — | 15,089 | 15,089 |
| Ovaries | — | 7,741 | 7,741 |
| Fallopian Tubes | — | 590 | 590 |
| Vagina | — | 131 | 131 |
| Labia Minora and Clitoris | — | 262 | 262 |
| Total | | 35,031 | 35,031 |
| **SYSTEMIC DISEASES** | 7,002 | 5,183 | 12,185 |
| Total | 7,002 | 5,183 | 12,185 |
| **METASTATIC CANCER (GENERALIZED) NO PRIMARY DISCOVERED** | 5,813 | 6,495 | 12,308 |
| Total | 5,813 | 6,495 | 12,308 |
| **GRAND TOTAL** | 128,113 | 150,051 | 278,164 |

Table II shows the estimated number of new patients with cancer in the United States in one year, by site and by sex. There are new improvements in therapy that will place many of these sites in the curable class. Adequate and early surgery or radiotherapy should remove the majority of the skin cases from the not cured category. The melanomas now being treated by radical removal stand a chance of years of health if not of permanent cure. Radical surgery in cancers of the skeletal system is saving some patients formerly considered beyond hope. Steadily improving pre-operative and post-operative care is increasing the chances of patients with digestive tract cancers. Cystectomy applied in time is already improving the prognosis for bladder patients. The concentration on improving the therapy for cancers of the upper respiratory and alimentary tracts is one of the most encouraging developments in the field. As recently as 1935 large series of patients at the community level were considered hopeless with relatively early cancers of the tongue, for example, because in the general practitioner's average practice, one is seen only about once in a lifetime, and groups of cures are seldom assembled, so with slight experience and the

best of intention, adequate therapy was not applied. These same practitioners are now attending teaching clinics run in their community hospitals, and seeing at first hand what may be done for patients with cancers of the tongue, gum or floor of the mouth. As this practice increases, the prognosis of the individual with cancer will improve.

The improvement possible for patients who have allowed the disease to progress is another encouraging development in the clinical research carried on at a specialized hospital. While it is realized that the American individual is bombarded with information about cancer, it is also known that symptoms without pain are still apt to be allowed to develop in many instances. The introduction of extreme radical surgery as a life saving technique in patients considered beyond hope was begun as the result of a study of a long series of autopsies of women with cancer of the cervix. It was found that in 50 per cent of all patients in this large series, who died from cancer of the cervix, the disease was still limited to the pelvis, and thus potentially amenable to cure by radical surgical intervention. There are an estimated 5,560 deaths annually in this category. If as many as half of these patients were cured by this admittedly radical surgery, 2,780 women now lost would be saved annually in the United States. These operations are being performed in gradually increasing volume, and have proved their merit in a number of women now ambulatory and restored to comfort, who would have died after a period of hopeless invalidism and discomfort.

A similar study of patients with cancer of the bladder showed at necropsy that, in thirty per cent of the series, there was no extension into adjacent structures. This means that of the 6,000 average annual deaths from cancer of the bladder in the United States 1,800 die without involvement of adjacent structures. If total cystectomy were performed in these cases and as many as half were cured, 900 individuals now dying annually could be saved.

These are two examples of which there are many, where sound consistent efforts in clinical research by responsible,

able men have shown what may now be done with available tools. While the research laboratories carry on without pause, and with encouragement, the clinical research and training has an immediate goal and stake in comfort restored and lives saved. Each new improvement in pre-operative care has been welcomed by the research clinician because it gave him a chance to try curative surgery with diminished risk to the patient. The responsibility of the clinical researchers is great. Each site must be explored for improvement in the techniques of therapy.

We can expect much in the hopeful beginnings in lung surgery, in stomach surgery, and even in surgery in the organs less often affected primarily, like the pancreas. The field is large and the workers are relatively few, but the rewards are high in life and comfort to infinite numbers of individuals.

How rapidly advances may reach the community level is largely dependent on how available the resources of the teaching and training centers become to the largest number of able men, and how tactfully and rapidly these trained men, when they return to their communities, may raise the therapeutic levels. There are many signs that this trend is in operation at this writing.

PRESIDENT DEWIS—Thank you very much, Dr. Rhoads. I am sure our audience was tremendously interested and that they have a lot of questions to ask you on that very interesting subject. Gentlemen, I am sure Dr. Rhoads will be very glad to answer any questions.

DR. CHARLES E. KIESSLING—Dr. Rhoads, do you have any follow-up studies on the cases detected early, in comparison with those that have developed symptoms of cancer?

DR. RHOADS—Yes, there are follow-up studies. There are official figures on the curability of early cancer as compared to curability of cancer encountered at routine admissions to institutions. One can review these figures quite easily. For example, all laryngeal—irrespective of degree of advancement—gives something under 20 per cent cure rates; while early laryngeal gives 70 per cent. Laryngeal disease usually can be detected early.

All breast cancers have an overall cure rate in the best hands of 31.5 per cent. Early breast cancer is now being cured in about 80 per cent of cases, or a little more, in good hands.

Cancer of the cervix has an overall cure rate of roughly 29 per cent. When discovered early, it has upwards of 80 per cent cure rates.

Others run along the same general way. There are one or two exceptions in forms of cancer which are not easily susceptible to early detection. I refer particularly to cancer of the stomach. Now all are actively seeking better methods, which means the routine x-ray studies of the pylorus in males over fifty, to obtain early diagnosis of gastric cancer. It is a difficult administrative job, but there are indications that it can be done effectively.

I refer to a paper by Harvey and St. John, of Presbyterian Hospital, New York, and to another paper from the Johns Hopkins Hospital. In males, by a spot film of the pylorus, early cancer was discovered in about one in every eight hundred apparently well individuals so screened. These early lesions usually are susceptible to cure. The reason the cure rate in general is so bad is that we get the patient late.

Another exception is cancer of the prostate, for which there has been no good procedure for early diagnosis. I am hopeful that investigations now under way in Oregon will result in a method of cytologic diagnosis which will allow routine examinations of the prostate for cancer. Examinations routinely of the prostates removed at autopsy by Rich and Hopkins and Moore in St. Louis reveal between 12 and 14 per cent of latent cancers. At present, we have no way of finding those, but I am sure a way can be found if adequate support of research can be instituted.

Dr. Graham, in a series of one hundred prostatic cases, found three suggestive of cancer, all three confirmed at radical operation. The prostatic cancers have the same curability as those of the cervix or breast through procedures that now exist.

DR. JOSEPH C. HORAN—I wonder if Dr. Rhoads would be willing to discuss the blood tests proposed currently and possibly in the future.

DR. RHOADS—Due, in my opinion, to an improper degree of pressure on investigators, there have appeared in the last few months a number of reports of what are called diagnostic tests for cancer. To my mind, the data presented do not justify the conclusion that a diagnostic test exists. For such a test one must have a reproducible procedure which is uniformly positive when cancer is present and uniformly negative when cancer is absent. None of the reports has included a sufficient number of patients with early cancer, properly described, with a positive test in the absence of symptoms or other signs of severe disease.

I am sure the questioner refers to the Huggins test because of the great publicity which has attended the publication of the report by that investigator. Repetitions of the observations, attempted by Humberger, Bodansky, Glass and by many others, indicate quite uniformly that the changes described by Dr. Huggins and Dr. Jensen, his associate, are to be found in a variety of illnesses other than cancer. Futhermore, apparently about 30 per cent of the patients with early cancer confirmed by histologic study do not reveal a positive test. I quote from literature which is now in press. Indeed, Dr. Huggins indicated at a public meeting in Boston last June, that he had not meant for this test to be considered as a diagnostic test for cancer, but rather as an interesting change of the plasma albumin which was found in association with cancer under certain circumstances. I think it will be found that other general biochemical changes hitherto described are subject to the same qualifications Dr. Huggins made regarding the publication under his name.

I do not know of any diagnostic procedure which will pick out cancer as cancer. A cytologic diagnosis in cervical disease is a very accurate procedure if properly done, but its applicability is limited because it requires observation of a vast number of negative smears and examining a great number of well individuals to find one positive smear. I have no

reason to doubt that this laborious technical enterprise can be shortened by methods which are now under study, but it has not been shortened so far. In our clinic, we must examine over three hundred cervical smears to find a positive one. That is a low incidence of positivity, because we screen our subjects very rigidly. Other clinics, notably Toledo, are running 1 per cent positives and that makes it worth while.

Routine photoroentgenograms of the chest will reveal neoplasms in the chest quite frequently. In a substantial number of patients coming under care for cancer of the lung, the lesions were found by mass survey of the chest, without complaint or symptoms on the part of the patient. I have already referred to the diagnostic x-ray tests of the pylorus, but general diagnostic tests to indicate "cancer" or "no cancer" are, so far as I am concerned, not yet at hand.

Dr. Harold D. Delamere—I should like to ask whether there is the same general trend in the ten-year cures as in the five-year cures. Have they been followed up as well for ten years?

Dr. Rhoads—I did not present the ten-year cures, but they have been followed up. I think you have called attention to a very important consideration underlying a vast amount of experimental work at our institution and also that of many other research establishments. There is a distinct incidence of recurrence or of new tumors after the five-year period. In the breast cancers, that figure runs in various reports from 5 to as high as 8 or 9 per cent, and sometimes even higher. The best evidence is that in most instances these are not recurrences but are new tumors, and really represent an intrinsic tendency of that particular patient to develop cancer.

Now, as you know from the observations of Warren and others, the incidence of multiple primary cancer, excluding skin, wholly independent of different cytological types and sites at autopsy, is about 7 per cent, or far in excess of chance occurrence. That fact, coupled with the so-called late recurrence, seems to me to indicate that there is a basic biochemical

disturbance of the body in these individuals predisposing to cancer of various anatomical sites. This should be susceptible to analysis, and very intense studies are under way at the present time to follow up that lead. However, the general trend is the same at the ten-year period. Early cancer can be cured, by and large, but if advanced it is difficult. The cure of cancer depends in a substantial way on the skill, knowledge, diligence, and attention of the person who is trying to cure it. The importance of the problem really justifies serious attention in terms of specialization, based on the evidence.

PRESIDENT DEWIS—Are there any other questions? If not, thank you very much, Dr. Rhoads.

Our scientific program will continue with a paper on "The Present Status of Antimicrobial Therapy," by Dr. Walsh McDermott, Associate Professor of Medicine, Cornell University Medical College. Dr. McDermott's entire medical career has been devoted to the study of infectious diseases and antimicrobial therapy. His eminence in the investigative field is attested by membership in the Association of American Physicians, and the American Society of Clinical Investigation, as well as in many other leading medical organizations. He is managing editor of the *American Review of Tuberculosis,* and Chairman of the Experimental Therapeutics Study Section of the National Institute of Health. We can anticipate that this presentation will closely correlate the research side of progress in antibiotics, as well as their clinical application. I am pleased to introduce Dr. McDermott.

# THE PRESENT STATUS OF ANTIMICROBIAL THERAPY

WALSH MCDERMOTT, M. D.

*Associate Professor of Medicine*

*Cornell University Medical College, New York, N. Y.*

The present status of antimicrobial therapy is characterized by two features: (a) the multiplicity of drugs; (b) the increased awareness of the vital importance of host mechanisms in the final control of infection.

The multiplicity of drugs has made it imperative that we establish a precise etiologic diagnosis in every patient in whom we are confronted with an infection. Yet, the fact of the matter is that rapid and precise etiologic diagnosis is by no means easy with our present methods. At this time, one of our greatest needs is better and, particularly, more rapid methods for the precise diagnosis of infectious diseases at the bedside.

Until now we have tended to compensate for a lack in such methods, at least in certain instances, by the administration of all of the available antimicrobial drugs. All of us can think of situations in which one, two, three, four, and possibly even five have been administered at one time. It is perfectly obvious, however, that we have reached the limit of this type of therapy, and we can no longer administer all of the available drugs because of the fact that so many of these drugs are being rapidly introduced into clinical practice. In other words, with antimicrobial therapy as with the rest of medicine, advances have tended to complicate the picture. Because of this increasing complexity, I thought it might be proper to limit my discussion to those aspects of antimicrobial therapy of timely importance, and hence a variety of different topics will be covered.

The first subject I should like to mention is the problem of drug-resistant microorganisms. It is well recognized that the individual cells of a particular bacterial infection may differ in their degree of sensitivity to a particular drug. If these drug-resistant cells acquire predominance in a particular instance of infection, the corresponding drug will become valueless. It is not always sufficiently emphasized, however, that for all practical purposes, the clinical importance of this phenomenon of drug resistance is limited to streptomycin therapy and to a few rarely encountered situations with penicillin therapy.

The two situations in which drug-resistant microorganisms may be a problem with penicillin are:

(1) A minority of staphylococcic infections, particularly the more indolent ones.

(2) Certain rare instances of bacterial endocarditis.

Other than in these two highly special situations, the phenomenon of drug resistance is not a problem in penicillin therapy. With streptomycin, on the other hand, the emergence to predominance of drug-resistant bacteria occurs almost invariably, provided unhealed lesions persist and that drug administration is maintained. The mechanism of this phenomenon has been clarified by the studies of Demerec, Luria, Hattie Alexander, and others. Briefly, the prevailing notion is that drug-resistant bacterial variants are born by a mutation-like process every so many generations. If they happen to be born into an environment which contains no drug, their unique drug resistance gives them no apparent advantage over their fellow-bacteria. Consequently, their survival or death depends upon the same factors as those which govern their fellow-bacteria.

In contrast, when drug-resistant variants, or mutants, are born into an environment containing a drug, such as is provided by a patient under treatment with that drug, their unique property of drug resistance then endows them with a tremendous advantage over their fellow-bacteria in the competition for survival. It should be emphasized that this

advantage applies only in relation to the drug. By that I mean there is no reason to believe that the drug-resistant bacteria are any more immune to the natural defense forces of the patient than are the other bacteria. If the infection is sufficiently prolonged because of general or local inefficiency of the patient's defenses, the drug-resistant variant eventually becomes the predominating member of the population. Thus, according to the prevailing concepts, the administration of an antimicrobial drug does not cause the phenomenon of drug resistance; it merely provides a set of conditions which allow it to happen. Moreover, as mentioned previously, virtually the only situations in which the phenomenon is of any real importance clinically are in streptomycin therapy and in the penicillin therapy of certain staphylococcic infections.

Consideration of the phenomenon of drug resistance leads naturally to the question of the simultaneous use of two or more antimicrobial drugs, so-called combined therapy. On theoretical grounds there is reason to believe that the administration of two antimicrobics, both of which are active against a particular infecting species of microorganism, might result in the prevention or postponement of the emergence of drug-resistant bacteria. The reasoning behind this theory—and it should be emphasized it is as yet unconfirmed clinically—is derived from the fact that a drug-resistant variant occurs only in every so many generations, and it is mathematically improbable that a varient resistant to two dissimilar compounds would occur during the course of treatment.

For example, if the chances for the birth of a sulfadiazine-resistant colon bacillus are one in a billion generations, and the chances for the birth of a streptomycin-resistant colon bacillus the same, the chances for the birth of an organism able to survive in a world containing both drugs would be the product of the two probabilities, or one billion times one billion. Actually, the mathematics sounds like a very large number indeed, but the difficulty lies in the question of how long it takes a billion times a billion generations to develop in human patients under therapy. This is not known, though several promising studies have already been done.

Until the validity of this theory is affirmed or denied by clinical trials, the reasoning behind it is sufficiently sound to warrant the use of combined therapy whenever the emergence of drug-resistant bacteria is a reasonable expectation and two effective drugs are available.

As mentioned previously, in penicillin therapy the only situations in which drug-resistant bacteria are a problem are with some staphylococcic infections and with a minority of the cases of bacterial endocarditis. Even in these two cases, it is by no means certain that penicillin-resistant infections appear during the course of therapy, as happens, for example, during the streptomycin treatment of tuberculosis. It is much more likely that these penicillin-resistant staphylococcic infections were resistant to the drug right from the start. It is not always remembered that from the very first introduction of penicillin into clinical practice certain staphylococcic infections were completely resistant to penicillin.

Today, in a large general hospital type of service the penicillin-resistant bacteremias actually outnumber the penicillin-sensitive ones. It must not be assumed, however, that this represents an absolute increase in penicillin-resistant staphylococcic infections. They may be revealed, so to speak, only because of the fact that the bacteremias formerly seen with an extensive carbuncle, or boils, or acute osteomyelitis are now rapidly controlled at the office or at the home by the prompt administration of penicillin therapy. So, all that filters through to the large general hospital are cases which are already resistant to the drug.

Regardless of whether the increase is more apparent than real, the fact of the matter is that these penicillin-resistant staphylococcic infections are indeed a problem. Almost invariably, they are the sluggish subacute type of infection and rarely, in fact not at all in our own experience, have such infections occurred with acute osteomyelitis or some acute highly invasive type of staphylococcic infection. Despite their subacute character, these infections are none the less fatal, and under the available antimicrobial therapy the results have certainly not been very satisfactory. In our own

hospital we now see perhaps three to five such cases a year, and recovery is more unusual than death. Two such cases are going at the moment and neither of them is showing any spectacular response to the administration of all of the available antimicrobial agents with which we are familiar.

When the *in vitro* penicillin sensitivity of such staphylococci is in the neighborhood of one unit per cc. or higher, as it almost invariably is, we administer routinely some other drug in addition to massive penicillin therapy. By that I mean at least ten million units a day by continuous intramuscular drip, and along with it three or four grams of dihydrostreptomycin intramuscularly, or three or four grams of aureomycin by mouth. Even with such therapy the results are by no means uniform, and one cannot guarantee control of an infection of this type. Fortunately, this is relatively rare.

In connection with the question of drug-resistant bacteria and combined therapy, a few remarks on the clinical usefulness of *in vitro* sensitivity tests are in order. The only infections in which *in vitro* penicillin sensitivity tests are of help are bacterial endocarditis and systemic staphylococcic infections. Even in these instances, when the identity of the infection is established it is more logical to proceed with antimicrobial therapy at once and adjust that therapy when the results of the *in vitro* tests are available.

Other than in these two instances, once the species or organism causing the infection has been determined the proper dosage of penicillin can be predicted with fair accuracy and *in vitro* tests serve no purpose. In streptomycin therapy, *in vitro* tests are not very helpful to the clinician except in the treatment of tuberculosis. In the more acute infections such as those of the urinary tract produced by the gram-negative bacilli, it is much more sensible to identify the organisms and start with streptomycin or aureomycin, and finally chloramphenicol. If B. vascularia persist four or five days, one can be reasonably certain that drug resistance has occurred. There is no point in holding up therapy in acute infection while testing the drug resistance; so, in general, it is seldom necessary to do *in vitro* drug-resistant tests except in those special situations.

The only other aspect of penicillin therapy requiring mention at this time is the question of the necessity for intrathecal administration of the drug in the treatment of pneumococcic meningitis. Many physicians not concerned with antimicrobial therapy do not appreciate that the results in treatment of pneumococcic meningitis leave a great deal to be desired. Until quite recently, the case fatality rate was in the neighborhood of 50 per cent which seems fantastic when one realizes how sensitive the pneumococcus organism is to penicillin. As everyone knows, there has been a great deal of debate as to whether or not it is important to give the penicillin intrathecally. Certainly it is important, or it would seem so from the observations, unless one uses relatively huge doses of penicillin by the intramuscular route. Dr. Dowling, of Washington, has introduced that method using a million units of penicillin intramuscularly at two-hour intervals without any intrathecal therapy, and the results of his treatment of pneumococcic meningitis are definitely superior to those of other investigators. Therefore, the fact seems well established that provided one gives enough penicillin by the intramuscular route it is not necessary to administer it intrathecally. The same is not true for streptomycin because obviously one cannot administer any given amount of streptomycin by the intramuscular route due to the toxicity of the drug. At present, it certainly appears that in the treatment of tuberculosis and meningitis it is essential to continue to administer streptomycin by the intrathecal route, though such is not the case with penicillin.

When streptomycin was first introduced into clinical practice, it became almost immediately apparent that the drug possessed two undesirable features. It is neurotoxic on prolonged administration and, as everyone knows, its therapeutic effectiveness is eventually nullified as a consequence of the emergence to predominance of drug-resistant strains of microorganisms. The latter phenomenon occurs only when streptomycin is administered for a sufficient period in the presence of unhealed lesions. If it resolves, the phenomenon will not occur. It was very soon found that both types of neurotoxicity, vestibular dysfunction and deafness, bore a

strict quantitative relationship to the amount of drug used, and appeared during the actual period of drug therapy. In a patient with normal kidney function, if the total daily dose of streptomycin is no higher than 20 milligrams per kilogram (or one gram in an average sized adult), deafness is not to be feared and the incidence of vestibular dysfunction is negligible.

Subsequently it was noted that the dihydro derivative of streptomycin is appreciably less neurotoxic but apparently is as active therapeutically as the parent compound. In general, the neurotoxicity produced by the derivative also bears a direct quantitative relationship to the amount given. In the original studies of the toxicity of dihydrostreptomycin, however, it was noted and emphasized that both vestibular dysfunction and deafness might first appear at an appreciable interval—thirty, sixty, ninety days after the cessation of drug therapy. In general, such instances of delayed appearance of neurotoxicity have been infrequent and have occurred only after the use of extraordinarily large doses of the drug.

Recently, however, there have been two localized outbreaks of neurotoxicity with dihydrostreptomycin following the use of the drug in only moderate sized doses. This experience has not been observed by other investigators throughout the country using the same lots of the same drug. It is not known whether these localized outbreaks which have not continued represent merely the effects of chance distribution or possibly that certain preparations of dihydrostreptomycin were more neurotoxic than others or became more neurotoxic, depending on their handling locally.

Pending more information, about all that can be said is that dihydrostreptomycin is definitely less neurotoxic than streptomycin, but the dihydrostreptomycin is by no means devoid of neurotoxicity. The occurrence of the reaction with it may be less predictable than with streptomycin.

The question of the relative merits of streptomycin and its dihydro derivatives actually resolves itself into the question of the *size* of the daily dose of streptomycin which will produce

the maximal attainable antimicrobial effect per unit of time. The one-gram daily dose of streptomycin is virtually free of serious neurotoxicity and undoubtedly produces significant therapeutic effects in all diseases caused by streptomycin-sensitive species of bacteria. However, the effects observed with this low dosage should not be accepted as representing the maximal attainable effects. If it could be shown that a two or three-fold increase in the daily dose of streptomycin were associated with a significant increase in therapeutic effectiveness, the use of the less toxic derivative would clearly be indicated.

Because of the many familiar variables, it is extremely difficult to measure degrees of clinical effectiveness from comparison of the courses of patients treated with various quantities of an antimicrobial drug. One reasonably precise type of observation which may be used in such a study is analysis of the pattern of the emergence of drug-resistant strains of microorganisms in patients treated on various dosage regimens.

The results of such bacteriologic studies in sixty-four patients with tuberculosis may be seen in Figure I.

The two rows of vertical columns represent two series of patients. The top row consists of thirty-three patients who received 3.0 grams of streptomycin each day.

The bottom row consists of thirty-one patients who received 1.0 gram of streptomycin each day.

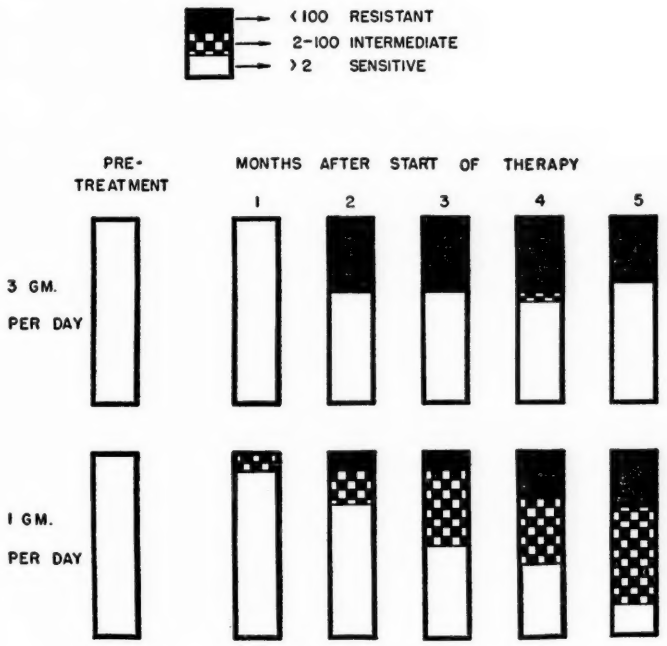
The individual columns represent the bacteriologic studies at monthly intervals after the start of streptomycin therapy.

Strains untouched by 100 micrograms per cc. of streptomycin are designated as completely resistant and are indicated in solid black.

Strains of an intermediate degree of drug resistance, that is, definitely more resistant than before treatment but not completely resistant, are indicated in black and white checks.

The strains with unchanged drug sensitivity are indicated in solid white.

COMPARISON OF THE EMERGENCE OF RESISTANT STRAINS OF M. TUBERCULOSIS ON TWO STREPTOMYCIN REGIMENS




(FIGURE I)

As may be seen in the left-hand column, all strains isolated from both groups before treatment were quite sensitive to streptomycin *in vitro*.

On both the 3-gram and the 1-gram regimens, highly resistant strains appeared during treatment—that is, the solid black—in approximately the same incidence.

The significant difference between the two treatment groups lies entirely in the incidence of strains with an intermediate degree of drug resistance indicated by the checkered areas. On one gram daily, these intermediate strains appeared early and their incidence steadily increased. In contrast, on three grams daily virtually all strains were either highly resistant or highly sensitive throughout a six months' observation period; in other words, the checkered areas represent a large number of tubercle bacilli which could be killed on three grams a day but were not killed on one gram a day.

The following interpretation has been made of these observations.

The precise degree of drug resistance that must be attained by the major part of bacterial population within the body before essentially complete nullification of streptomycin activity occurs is not known. Nevertheless, when one bacterial cell with increased resistance to a drug—in this case streptomycin—is born, the effectiveness of streptomycin in that particular infection has been compromised by that little bit. When the survival of bacteria of an intermediate degree of resistance is prevented, the curve of antimicrobial activity persists at a high and more or less horizontal level. This continues until sufficient time elapses for the highly resistant organisms, which are fewer in number, to multiply to the point of taking over the infection, and at that point the therapeutic effect falls off sharply.

In clinical experience with tuberculosis, that period is approximately ninety days. In contrast, when the survival of bacteria of an intermediate degree of drug resistance is favored, as is the case on one gram daily, the curve of drug activity—the number of organisms being killed off in proportion to those present—is a slanting diagonal with a steady fall-off from day to day, or week to week, from the very beginning of therapy. It is most unlikely that such a steady slanting fall-off in drug activity would ever be appreciated by the relatively crude clinical and roentgenologic methods at our disposal for the observation of tuberculosis.

On the basis of this interpretation of the bacteriologic observations, it would seem advisable to adopt one of two alternatives in the streptomycin treatment of each patient with a chronic infection such as tuberculosis. In instances where the disease constitutes a clear and present danger such as miliary tuberculosis, extensive pneumonia, and the like, a large daily dose of streptomycin or dihydrostrepomycin should be used for a period of three or four months. In this situation, the eventual nullification of drug activity and some incidence of neurotoxicity would simply be accepted as inevitable. In those other forms of tuberculosis in which the prognosis without antimicrobial therapy is reasonably good, streptomycin should be used only as an occasional adjunct to the powerful defense mechanisms of the patient by administering the drug once, or at most twice, each week. This hit and run therapy eliminates the environment which favors propagation of the intermediate resistant organisms. In this way, some of the admittedly therapeutic benefits can be obtained without continuously providing an environment of that kind.

From theoretical considerations mentioned previously, there is reason to believe that the administration of another effective antimicrobial drug along with streptomycin might appreciably postpone or prevent the emergence to predominance of these drug-resistant organisms. As I said before, there is surprisingly little clinical evidence to affirm or deny that hypothesis. From studies in the Veterans Administration, it seems clear that the various sulfones, such as promizole, when administered in conjunction with streptomycin have no influence on the emergence of streptomycin-resistant tubercle bacilli.

In contrast, on the basis of preliminary observations by D'Esopo and Hinshaw, their associates, and our own group, it appears that paraamino salicylic acid administered along with streptomycin may significantly postpone but not prevent the emergence of drug-resistant organisms. By this method, it appears possible to prolong by a period of several months the period during which the streptomycin activity can be maintained.

The use of another antimicrobial drug concurrently with streptomycin for the purpose of attaining an additive therapeutic effect may represent a slightly different aspect of this same general question. The use of sulfadiazine and streptomycin in brucellosis by Spink and his associates is a good example of this type of combined therapy. That particular form of treatment has now been superseded recently, and more recently Robbins and Tompsett of our own group have been studying combined therapy in the treatment of bacterial endocarditis caused by enterococci.

It is not always appreciated that in approximately 10 per cent of the patients with streptococcic endocarditis death occurs as a direct result of failure to control the disease with penicillin. The majority of these patients are infected with enterococci which are relatively resistant to penicillin. Penicillin and streptomycin are each capable of exerting some effect on such infections, but sustained cures with penicillin alone are decidedly unusual. Both successes and failures from the use of streptomycin alone have been reported, but here, as with streptomycin in other infections, the emergence to predominance of drug-resistant bacteria has been observed.

Thus far in the Robbins-Tompsett study eight patients with persistent enterococcic bacteremia and enterococcic endocarditis have been treated with penicillin and streptomycin or its dihydro derivative. Two of the eight patients received only a few days of streptomycin therapy just before death. The remaining six patients received longer periods of treatment and are all alive and well. As to remissions, in all but one the patients have been maintained for more than one year.

One patient was a 60 year old man with enterococcic endocarditis. The strain of enterococci required 6 units per cc. of penicillin, or 8 micrograms per cc. of streptomycin for inhibition *in vitro*. I think anyone will agree that organisms that will increase with six units of penicillin, even 10, 20, or 30 units seldom accomplish anything in the treatment of such infection. This patient received only 6 million units of penicillin and two grams of streptomycin daily for twenty-eight days. Reversal of bacteremia and return of the temperature

to normal occurred, and the status has been maintained in this particular patient for over two years.

Although six recoveries from enterococcic endocarditis are most gratifying to see, it should be emphasized that it is still unsettled whether the successes are due to the actual combination of the therapy or to the use of streptomycin. It is known that penicillin in that amount will not do it, but it is not known whether the streptomycin alone would do it. Unfortunately, I think we will never know the answer to that because, as a consequence of the known danger of the emergence of streptomycin-resistant organisms, no one will try a series of patients on the one drug alone. About all that can be said is that these results are most gratifying indeed from the clinical standpoint. We believe they represent the consequences of the added effect of the two drugs, but the point cannot be considered as absolutely established.

During the past eighteen months, a considerable experience has been accumulated in the treatment of a variety of infections with the use of aureomycin, or Chloromycetin®, or chloramphenicol as it is known by the generic name. As a consequence, we are all generally familiar with the use of these two drugs, their indications and effectiveness, in a majority of infections seen in these parts. Consequently, I thought it might be of interest to discuss the use of these drugs in three important infections which are relatively seldom seen, at least in these particular parts of the country.

During the last half of 1948 and the first part of this year, our group at Cornell conducted a joint investigation with the University of Guadalajara, in Mexico, on the use of chloramphenicol or aureomycin in the treatment of three infections: typhus, brucellosis, and typhoid fever. Twenty-eight patients with typhus fever, presumably of murine variety, were treated with aureomycin. The first twenty-three of these twenty-eight patients received oral doses of the drug and more than three-quarters of them received a dosage regimen of 150 to 200 mg. per kilogram per day for periods ranging from only twenty-four to forty-eight hours. Improvement was almost

invariably noted within twelve hours after starting therapy, and within forty-eight hours virtually all patients were permanently afebrile and convalescent.

Twenty-five patients with acute brucellosis received aureomycin or chloramphenicol, approximately half and half. The diagnosis was made by the demonstration of positive blood cultures in about half the patients and significant rises in antibody titer in the other half. All of the patients were acutely ill at the time therapy was started, so they would be classified as acute brucellosis. Various degrees of severity of the infection appeared between the two groups but on the whole they were comparable. Moreover, the doses of aureomycin and chloramphenicol used were comparable and consisted of 50 to 100 mg. per kilogram per day, three to six grams a day, with lower doses once defervescence had occurred.

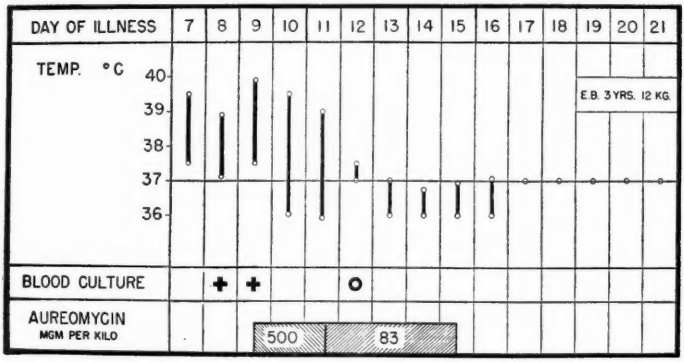
The treatment period was all too short and ranged from in the neighborhood of ten days to sometimes as short as eight days. The clinical response to therapy with both these agents was excellent. By the second or third day almost all patients were afebrile and showed great symptomatic improvement. The joint pains and other manifestations disappeared promptly and all of the patients, even the most severely ill, were ambulatory by the end of treatment.

If the courses before the start of treatment are considered, there was no evidence from this study that either drug was superior to the other in the treatment of acute brucellosis, and there was every reason to infer that they both were highly active. The follow-up observations of these patients, however, have shown a high incidence of relapse following both drugs, and it is to be hoped that with more intensive therapy or much greater prolongation of therapy, perhaps up to five or six weeks, the incidence of relapse may be sufficiently diminished.

Fifty-one patients with typhoid fever were treated, thirty-five with aureomycin and the remainder with chloramphenicol. Eight per cent of the entire group where bacteremic and the others

all developed a significant rise in antibody titer. In approximately one-half of the total series, therapy was started before the twelfth day of illness. The aureomycin and the chloramphenicol were both given orally and the aureomycin usually in the amount of six to twelve grams a day, although in some instances as much as eighteen to twenty-five grams per day were given. In the aureomycin series, two of the thirty-five patients died as a result of intestinal complications. The remaining thirty-three recovered and none developed any of the familiar complications of typhoid fever. The most rapid recovery in the aureomycin series was illustrated by a three year old child, bacteremic on the ninth day of illness when therapy was started. In the bottom half of the Figure 2 is the type of course seen in approximately two-thirds of the patients who received aureomycin. After forty-eight hours, approximately two-thirds of them seemed a little better, but defervescence was not prominent and the symptoms persisted, and the patients were not completely afebrile until the end of one week.

AUREOMYCIN IN TYPHOID FEVER



In one-third of the patients receiving aureomycin, there was complete therapeutic failure. There was no evidence of remission, although the drug was administered in large doses relatively early in the disease. There was no evidence that it had any effect on the course of the infection. Thirty-three of the thirty-five patients who received aureomycin made uncomplicated recoveries, but the pattern was not uniform and was not certainly attributable to the action of the drug.

In contrast to the irregular pattern with aureomycin, the results following chloramphenicol were uniform and striking. They were in complete agreement with the previous records of Woodward, Smadel, and their associates. Fifteen patients, twelve with bacteremia, were started on chloramphenicol between the fifth and nineteenth days of illness. The regimen generally used consisted of 100 milligrams a day of chloramphenicol per kilogram, orally, for the first few days and much smaller doses thereafter. Regardless of the previous duration of illness or the presence or absence of bacteremia, the average period of fever and symptoms after the start of chloramphenicol was 3.2 days, and there were no deaths.

A 19 year old man had ten epistaxes and constant delirium, with marked tremor of the extremities, during the third week of a bacteremic typhoidal relapse. A large intestinal hemorrhage was heralded by a sharp fall in temperature and was followed by characteristic signs of intestinal perforation. Gross soiling of the peritoneal cavity was found at operation, and a perforation of the ileum was sutured. Chloramphenicol was started one hour postoperatively, and no other antimicrobial therapy was used. Only slight improvement was evident in forty-eight hours, but he improved rapidly thereafter. By the fifth postoperative day he was rational and completely asymptomatic.

A 14 year old school boy was critically ill on the eighteenth day of bacteremic typhoid when chloramphenicol was started. During the first forty-eight hours he showed no improvement. His temperature remained high, his delirium continued, and severe and apparently painful abdominal distension persisted. During the third day of therapy, abrupt defervescence oc-

curred. Over-night his abdominal distension disappeared and he became alert, cheerful, completely rational, and hungry. The remission was maintained.

One striking phenomenon was the fact that during the first forty-eight hours of treatment there was not the slightest indication of any improvement. During the next twelve to twenty-four hours the improvement occurred in the form of a rapid crisis with dramatic abruptness. It is possible that the delayed appearance of any improvement represents a lag in the disposal of the endotoxin formed by the parasites.

Relapse occurred in three of the thirteen chloramphenicol cases and in seven of the thirty-two aureomycin cases, an incidence for each drug which is essentially the same as in untreated typhoid fever. Dr. Smadel's recent work seems to show that prolongation of therapy up to three or four weeks may completely or materially reduce the incidence of relapse.

In summary, aureomycin appeared to have some effect on the course of typhoid fever, particularly in the early cases, but the results were seldom dramatic and sometimes were negligible. In contrast, the administration of chloramphenicol was uniformly followed by a complete remission of the symptoms, usually by the end of the third day of therapy.

PRESIDENT DEWIS—Discussion of this most instructive paper will be opened by Dr. Joseph W. Johnson, Jr., who is the Medical Director of the Interstate Life and Accident Company of Chattanooga. In addition to his valued membership in this Association, Dr. Johnson is an internist of note in his own right. He is Visiting Physician to the Pine Breeze Tuberculosis Sanitarium and Consulting Physician to the T. C. Thompson Children's Hospital in Chattanooga, among other local and national affiliations. During the recent war, he served as Lieutenant Colonel in the Army of the United States and during part of this period acted as instructor in medicine at Vanderbilt University. It is my pleasure to introduce Dr. Johnson.

DR. JOHNSON—Dr. McDermott has given us in his usual, delightful and lucid fashion just exactly what his paper prom-

ised in its title, "The Present Status of Antimicrobial Therapy". To discuss that paper from the point of view of our specialty of Insurance Medicine requires recognition of several factors:

1. Dr. McDermott's paper represents a *distillate* of the best contemporary knowledge concerning a subject which has favorably influenced our experience with disability and death and apparently will continue to do so.

2. Insurance medicine, however, requires a *diffusion* of such knowledge among the practitioners of medicine who care for our policyholders and acceptance of proper therapy on the part of an informed population.

3. Diffusion of knowledge critically arrived at almost invariably involves certain uncritical usages and always involves a factor of time for diffusion which may be extremely variable.

4. Underwriting human disability and death caused by microbes requires a knowledge of the broad strategic gains and losses of antimicrobial warfare, as well as such tactical opportunities as are afforded by antimicrobial therapy.

Over the years, insurance medicine has had to observe and appraise rather gingerly many of the earlier antimicrobial efforts. Quinine, mercury, antimony, arsenic, and other agents have served usefully and still so serve, favorably influencing disability and death caused by microbes. Indeed, since it was established that disability and death could be caused by microbes, the latter have been set upon by dyes of variegated hues, various wavelengths of the electromagnetic spectrum, other microbes, and products resulting from the interactions of microbes and hosts, there being practically no limit to the impositions imposed upon microbes. There have been brief periods of enthusiasm for accomplishments, inadequately controlled, but slowly and impressively there resulted accomplishment. I think it is fair to say, however, that so far as the years prior to 1937 are concerned, the great accomplishments represented by decreasing mortality and disability from

microbial diseases, bear tribute to preventive medicine and socio-economic factors rather than to antimicrobial therapy.

It is not altogether fair to say that the Metropolitan's report, "Twenty-Five Years of Health Progress," 1911–1935, represents progress without antimicrobial therapy; but it is correct, I believe, to say that antimicrobial therapy came into promising being only after the Dublin study.

Less than a decade ago, at the 1940 meeting of this Association, Dr. Chester Keefer, presented "The Present Status of Chemotherapy in the Treatment of Infections", wherein he said, "During the past 5 years we have all witnessed great changes in the treatment of infectious diseases. These advances have been due in large part, to the introduction of three drugs. They are: (1) Sulfanilamide, (2) Sulfapyradine, and (3) Sulfathiazole." Dr. Keefer's conclusion that "we may look forward to other advances in the near future" has certainly been fulfilled in the addition of new sulfonamides and the antibiotic drugs to our antimicrobial therapy.

Though that was the era of "Sulfa-Miracles", Dr. Grant Irving's discussion of Dr. Keefer's paper "indicated the serious toxic effects of sulfamido compounds", offered a plea for further research, for "control of the distribution of such potent drugs" and presented "a series of charts and tables to indicate the apparent success of the compounds in reducing the mortality and morbidity of certain diseases".

Today, the three sulfonamides that Dr. Keefer mentioned have largely been replaced, and Dr. McDermott offers us four new antimicrobial agents with impressive clinical evidence of their effectiveness and safety.

These agents are penicillin, streptomycin (and its newer dihydroxy-streptomycin), aureomycin and Chloromycetin® or chloramphenicol. Penicillin was almost immediately seized upon as another "magic drug". While its effective limitations were early recognized, it nonetheless has been and still is sometimes used almost as an antipyretic by uncritical individuals. Because it is safe and increasingly inexpensive, such usage was understandable. The aura of magic about this

drug is interesting. It was so impressive during its early use in wartime Italy that "Axis Sally" and German propaganda shells pounded away on the thesis that penicillin rendered patients sterile and impotent. It might be said that as knowledge of penicillin's effectiveness first diffused throughout the Army and the general population bacteriologic diagnosis briefly suffered. However, as limitations became increasingly apparent in terms of specific bacteria, new antibiotics were sought to deal with specific penicillin failures.

Streptomycin was the first of these to show general promise and to offer the challenging possibility of being effective in tuberculosis. Streptomycin also offered the first serious complications attributable to an antibiotic, the eighth nerve damage already referred to by Dr. McDermott. This seems to have been largely offset by the use of dihydrostreptomycin and a more judicious dosage administration of the drug. Certainly streptomycin has proved life saving in hemotogenous and meningeal tuberculosis, and alone or with the use of paraamino salicylic acid, and perhaps one of the sulfones, is proving increasingly useful in the treatment of pulmonary tuberculosis. The combined use of streptomycin and sulfadiazine has proved useful in brucellosis, while employed with penicillin it has been useful in subacute bacterial endocarditis caused by enterococci. Streptomycin has also demonstrated its usefulness in plague and in those urinary infections with pyocyaneous oganisms and Proteus when complicated by bacteremia. In short, the advent of this antibiotic necessitated more discriminate bacteriologic diagnosis.

More recently still, aureomycin and Chloromycetin® have been given us. These have proved even more effective against the gram-negative bacillary infections previously best treated with streptomycin. Of these Chloromycetin® seems most effective in typhoid fever; but most encouraging is the increasing evidence that the barriers which have hitherto been imposed between effective antibiotic therapy and the virus diseases are being breached. Certainly, aureomycin has given impressive evidence of its effectiveness in the symptom complex known as atypical pneumonia and shown promise in the

psittacosis-lymphogranuloma group. In the rickettsial infections, aureomycin has proved effective in Rocky Mountain spotted fever, typhus, either proved or presumed to be of the murine type, and Q fever. Both Chloromycetin® and aureomycin appear to be equally effective in brucellosis and, perhaps, more effective than the streptomycin-sulfadiazine combination. Patients with tularemia have responded to aureomycin in a manner comparable to that of streptomycin. Dr. McDermott, in a letter to me, raised a point regarding the conflicting reports of aureomycin's effectiveness in infectious mononucleosis. Dr. Jack Adams, pathologist of our local general hospital, informally reported to me that he had seen some 12 cases well established by laboratory means as infectious mononucleosis which, seemingly, have responded dramatically to aureomycin. An example was a 21 year old white male with fever, malaise, and sore throat for four days. Temperature on the fourth day was 103 F. There was generalized lymphadenopathy, a palpable spleen, low titer heterophile and typical smear. Treatment with aureomycin was begun and fever dropped to normal with 48 hours, glands disappearing within the next week, and heterophile rising to positive in the 9th tubes.

The point I would make here is that new antimicrobials are available. Their usefulness and their limitations are in the process of definition and, by virtue of their specificities, accurate bacteriologic diagnosis is necessary. We have four new weapons; but may I stress, again, that, like Dr. Keefer's three new weapons presented in 1940, which have already been displaced, these are tactical weapons.

A point was made somewhat earlier in my discussion that insurance medicine requires a diffusion of knowledge of these tactical advances in order that they may be generally available to our policyholders. It was mentioned, too, that diffusion of such knowledge involves both uncritical usages and a matter of time. It would seem to me that a basic function of the medical directors and their staffs is to aid in such diffusion through active participation in the professional activities of their individual communities. And in order that the broad

strategic gains in antimicrobial warfare may be supplemented by antimicrobial therapy, it would seem, too, that the medical director must maintain at least an active interest in public health programs and community health problems on an educational level.

Our specialty in medicine is a particularly interesting one, for the very nature of insurance is based upon judgment and prognosis. It involves continuity, based on objective trends—what I have referred to as the strategic gains in medicine. But because insurance also involves competition, there is no use pretending that medical directors can sit in an ivory tower lit by the thin white flame of science and calculate risk with a slide rule. Competition between companies, the pressure of agency departments, the desire to broaden the base of substandard risks through knowledge, make it necessary for the medical director to be informed of the best contemporary knowledge of medicine. It is this contemporary knowledge or what I have referred to as tactical gains in medicine, that makes competition possible, broadens the base of substandard appraisal, and allows insurance medicine to grow shoulder to shoulder with contemporary medical knowledge.

I wish, therefore, to express my thanks to Dr. McDermott for a paper which brings to us clearly the best contemporary knowledge of antimicrobial therapy, and to express also my gratitude for the privilege of discussing his paper before you.

PRESIDENT DEWIS—Thank you very much, Dr. Johnson. I am sure there must be a number of questions you would like to ask Dr. McDermott or Dr. Johnson.

DR. HUGH B. CAMPBELL—May I ask Dr. McDermott if he is convinced that the later procedure of assumedly treating more acute tuberculosis with aureomycin and streptomycin is sound, in view of Dr. Archibald's recommendations as to treatment and views on thoracoplasty.

DR. MCDERMOTT—I am summarizing. The question is whether it is a good idea to use thoracoplasty in acute cases of tuberculosis, a procedure which is made possible by the use of streptomycin, or whether it is not better to follow the original

recommendations of Dr. Archibald that thoracoplasty should be used only for reasonably established lesion. Is that a fair summarization?

DR. CAMPBELL—Especially in view of the fact that only time will tell whether we are warranted in proceeding as at present.

DR. MCDERMOTT—I can say, in answer to the question, I am in complete agreement with Dr. Archibald. Certainly, covering an acute case of tuberculosis with antimicrobial therapy and then doing a thoracoplasty seems to me to be very much like sweeping dirt under a rug. The acute nature of the lesion is still present, even though one were temporarily able as a surgical feat to collapse it. I think streptomycin has aided surgery in the conversion of acute cases to the subacute or chronic ones before the thoracoplasty is ever started. In other words, it brings more people into the group which Dr. Archibald would consider as proper for thoracoplasty.

DR. E. CLARK NOBLE—I wonder if Dr. McDermott would say something about the sensitivity of the drugs, particularly penicillin.

DR. MCDERMOTT—Untoward reactions of these drugs?

DR. NOBLE—Yes.

DR. MCDERMOTT—Taking it up backwards, so far as chloramphenicol and aureomycin are concerned, other than the known gastric irritation, particularly from aureomycin, which is extremely variable from patient to patient, and completely unpredictable, those drugs have not seemed to be a problem. Although I am sure that hypersensitivity reactions occur, they certainly have not seemed to be a problem to date.

So far as streptomycin is concerned, certainly hypersensitivity reactions occur; frank ones occur in some 3 or 4 per cent of the cases. A portion of those cases are not equally sensitive to dihydrostreptomycin but, conversely, some patients are hypersensitive to dihydrostreptomycin.

So far as penicillin is concerned, hypersensitivity reactions are a problem. I do not know whether it is superstition or

not, but it always seems to me they are more of a problem when there is doubt about the indications for giving it in the first place. It is always the man who got penicillin so he could make a speech at the alumni dinner who gets the terrific reaction in the joints and gets hives and is laid up three or four weeks, in contrast to the critically ill patient who escapes these reactions.

Hypersensitivity reactions are a problem and the only way I know of handling them is simply to accept the fact when administering any of these drugs that they possess a potential toxicity. The chances of potential toxicity must be weighed against the chances of threat from disease.

I think, in consideration of Dr. Johnson's remarks, that on a broad philosophical level the point you have raised is a very important one to this group. I think it is almost definite that the incidence of periarteritis nodosa, for instance, was higher in the Army experience during extensive use of the sulfonamides. Now we do not know whether the incidence of the whole group of vascular diseases is on the increase, although it certainly seems to be. Nor do we know that it bears any real relationship to all the agents we are pouring into people, but at the moment there is a well-founded suspicion that such is the case. It might well be that in the future—I am talking in terms of decades, not in terms of years—we might find serious changes in our death rates as a consequence of the widespread use of drugs causing hypersensitivity reactions at the present time, but that is entirely philosophical and there is no evidence to back it up.

Dr. Paul H. Langner, Jr.—I should like to ask Dr. McDermott what the present status of caronamids is in conjunction with penicillin, and, secondly, how much do the antibiotics alter the natural immunologic response?

Dr. McDermott—So far as caronamid is concerned, it is an extremely difficult technical feat to get enough penicillin into somebody whose organism requires, let us say, one, two, or three or four units of penicillin per cc. It is extremely difficult, particularly in the resistant Staphylococci, enterococci,

and so forth, to get in 20 or 30 milliunits of penicillin a day. It is conceivable in such a case that the use of caronamid might be of help. Only in that situation would it really be of help—that is, in organisms that are very highly resistant to penicillin. In all other situations it seems much more practicable simply to give more penicillin rather than to give large quantities of another drug which also has its own toxicities.

So far as the second question is concerned, these drugs in most instances alter the immunologic response. There is one situation in particular where one very obviously can interfere with host immunity and that is in streptococcic sore throat. Certainly here, if one administers penicillin for a period of three or four days and then stops, the patient may be left in worse shape than if no penicillin had been given, from the standpoint of host immunity. Patients often receive a short course for streptococcic sore throat, followed by a relapse and retreating, then another relapse and retreating, and finally penicillin is discontinued and the patient is allowed to try to get better without it. The way to prevent relapses is to administer ten or fifteen units of penicillin a day to every patient with streptococcic sore throat.

From the work of Kilborne, and Logc, and Wagenstein, in Boston, there is reason to believe that by early penicillin therapy in the course of the streptococcic sore throat it might be possible to suppress humoral antibody formation on the Streptococcus. As we all know, there may be some relation to such humoral antibody in the incident of rheumatic fever and glomerular nephritis; so there is one place where it is possible to alter immunity. In the other infections I do not think it can be altered once the infection has progressed to the point of clinical recognition.

Dr. Verne S. Caviness—I should like to ask Dr. McDermott how long the drug resistance is likely to persist in bacterial endocarditis and in staphylococcic infections, following stoppage of the use of the antimicrobial therapy.

Dr. McDermott—I suspect in the staphylococcic and bacterial endocarditis most of those are resistant from the start and continue to be resistant indefinitely. In those developing

resistance during therapy, such as the tubercle bacillus or gram-negative infection in the uninary tract, I think it is more or less a question of the speed with which the particular organisms naturally reproduce. Where only forty-eight hours are required for an infection to become completely occupied with resistant cells such as urinary tract infection, I would anticipate a period of one or two weeks as sufficient for it to go the other way. But, once the infection of tuberculosis has become predominantly resistant, it is resistant permanently, or for a period of a year or two, which is all that is necessary to compromise therapy in the individual patient.

PRESIDENT DEWIS—Thank you very much, Dr. McDermott and Dr. Johnson. The next paper is entitled "Surgical Treatment for Coarctation of the Aorta," by Dr. Robert E. Gross, Ladd Professor of Children's Surgery, Harvard Medical School.

We are very fortunate in this opportunity to hear a presentation by a surgeon of international reputation who has contributed so much to the development of operative technics greatly improving the life expectancy of those with various types of congenital deformities of the cardiovascular system. His many papers in the medical literature on these subjects are well known to all of you. I need only mention that in addition to his professorship, Dr. Gross is Surgeon-in-Chief of the Children's Hospital and Associate Surgeon to the Peter Bent Brigham Hospital in Boston. He is a fellow of the American College of Surgeons and of the American Association for Thoracic Surgery, and also participates in activities of other medical organizations, his interest in the research aspect of his specialty being shown by membership in the American Society for Experimental Pathology and the American Association of Pathologists and Bacteriologists. We are all very happy to welcome Dr. Gross.

# SURGICAL TREATMENT IN ONE HUNDRED AND THIRTY CASES OF COARCTATION OF THE AORTA

ROBERT E. GROSS, M. D.

*Ladd Professor of Children's Surgery, Harvard Medical School. Surgeon-in-Chief, The Children's Hospital, Boston, Mass.*

Obstructions of the aorta can occur at any level. They may appear in the abdominal or lower thoracic portions, but they are extremely rare in those positions. The vast majority occur just below the origin of the left subclavian artery, or within a segment a few centimeters distal to this region.

Aortic obstructions carry a variable prognosis. From a study which we have made, it is evident that these patients could be divided into four groups:

In the first quarter (26 per cent) were those humans who lived a rather long life and had little or no trouble from the aortic block. Some of them had symptoms which took them to a doctor, but on the whole they got along faily well. Many of them lived to advanced ages. These observations emphasize the fact that aortic obstruction, even of high degree, can be tolerated in a certain percentage of people in a reasonably satisfactory way through six or seven decades or more.

In the second quarter of the patients (23 per cent) there was sudden death from aortic rupture. Rupture rarely occurred in childhood or in later life. When it did appear, it usually came in the twenties or thirties. The aorta can rupture either above or below a block. These lesions usually do not lead to dissecting aneurysms with a continuance of life over a period of time; as a rule, exodus is sudden. While one might assume that disruption would be most prone to occur above the obstruction, where the thrust is most intense, actually a large number of the ruptures occur below the narrowing. This is probably related to the fact that the aorta, and especially the intercostal arteries (as they enter the distal

aorta), are apt to be thinned out and will rupture even though they are subjected to a pressure which is lower than that in the arch.

In the third group (22 per cent) there was death from bacterial infection. Vegetations formed in the region of the constriction, though some of them had a earlier start on some other anomalous structure such as a bicuspid aortic valve. Streptococcus viridans infections are obviously not so much of a threat today when the various chemotherapeutic agents are available to us.

In the final group (29 per cent) there was death from the hypertensive state, exodus coming either from congestive cardiac failure or from intracranial hemorrhage.

In summary, while it is true that certain people tolerate a coarctation through a long life, there is overwhelming evidence that the possessor of an aortic obstruction carries a high risk of serious complication or death from the lesion. The condition often goes unrecognized and has little symptomatology for ten to twenty years, yet the anomaly is one which extracts an enormous toll in midlife. As is well known, the general population has death rates which are low between the ages of fifteen and thirty years. In contrast, if one studies a series of people with coarctation, a high mortality rate is found in this age group; about 40 per cent of the subjects apparently die in this period.

In a human with coarctation, the physical findings are such that the physician can quickly detect the presence of an aortic block by very simple and inexpensive means. The most important finding is the disparity in pulsations and pressures between the arms and legs. Normal persons should have a higher pressure in the legs than is found in the arms, whereas the presence of an aortic block will reverse this relationship. It takes but a few moments to feel for the pulsations of the femoral arteries. If these are diminished or absent, the pressure in the legs should be checked with a sphygmomanometer. Certainly, any patient with hypertension in the arms should have the leg pressures recorded, for in this way it is

possible to determine very quickly whether an aortic block is the cause of the high pressure in the upper part of the body.

Murmurs are extremely variable in appearance, in characteristics, and in points of maximal intensity. A few patients have absolutely no murmur. Most commonly, there is a systolic murmur of mild or moderate intensity over the precordium, transmitted with about equal intensity to the back, though in some it is slightly louder in the back. In occasional patients there is a continuous murmur which may arise from a patent ductus arteriosus or from a continuous rushing of blood through large collateral channels over the shoulders and back. There may be murmurs from associated intracardiac valvular deformities.

In children there may be little physical evidence of collateral circulation, but beyond 10 or 12 years pulsating vessels can usually be seen or felt above and below the clavicles, over the shoulders, in the axillae, and especially over the back. These are most easily detected in thin individuals, and conversely may be difficult to find in stocky or well nourished subjects.

It is surprising to find how often coarctation is overlooked in childhood, even though there may have been examinations by several physicians. A soft murmur is passed off as being insignificant and it assumes no importance until it is coupled many years later with other abnormal findings. There may be headaches, epistaxis or leg pain, the latter being brought on by exercise. Limitation of physical activity because of cardiac symptoms seldom appears before adolescent or adult years. Hypertension is frequently recognized by physicians, but the cause for the increased pressure may elude detection for years simply because the examinations have not been carried below the waistline. Cardiac failure, intracranial hemorrhage, or bacteremia may appear in persons who were previously thought to be in good health, but these complicating disorders then lead to a thorough evaluation of the patient and detection of his underlying vascular disorder.

Electrocardiographic tracings are of considerable importance in estimating the extent of damage which the heart may

have sustained. The hypertension found in most people with aortic block naturally places a burden on the left side of the heart. Some degree of hypertrophy is frequently found, and in adult life evidence of left ventricular strain is often observed.

By roentgenologic examination, the heart may be found slightly or moderately enlarged, depending upon the degree of hypertension and the length of time it existed. The aortic knob is small, or sometimes the roentgenologist reports that it is "absent". If the patient happens to be turned in just the right direction and the aortic shadow is thrown off the spine, the constricted area in the aorta may be seen, though there are many instances when it is not possible to make this observation. The most important finding is the notching along the inferior borders of the posteriolateral portions of the ribs. These erosions come from pulsation of the subjacent, dilated, intercostal arteries; their presence is diagnostic of an aortic block. There is an occasional adult in whom these notches do not appear, in spite of the fact that there are other evidences of a high degree of aortic obstruction.

We can get additional evidence regarding this anomaly by the injection of 70 per cent Diodrast. This can be given intravenously, or can be injected in a retrograde manner into the cervical or axillary arteries. We have found that intravenous administration of the dye can give a clear picture of the aorta and its obstruction, but that not infrequently the dye is so diluted by the time it reaches the aorta that one obtains only disappointing visualization. Under such circumstances, retrograde injection of the material down one of the major arteries may help. We have had the best luck by making a small incision in the left axilla, opening the axillary artery, and then threading an opaque catheter back through the vessel toward the heart. When the aorta is reached, the Diodrast is introduced and appropriate film exposures are made. While arteriography is helpful in some cases, it is not necessary as a routine work-up of cases; indeed, we do not employ it in the vast majority of cases which now come to surgery.

When I first initiated studies in the possibilities of surgical attack on coarctation a decade ago, it was almost heresy to think of sectioning and resuturing an artery the size of the aorta in the chest. Hence, it was necessary to turn to the laboratory to see what could be accomplished in the way of handling such a large vessel. It was important to learn whether or not the aorta could be raised from its bed, could have a piece removed, and could be reconstructed by direct suture of its remaining ends. With a series of dogs, these various steps were practiced. I will not enumerate here all the methods of arterial anastomosis which were studied, but will summarize results by merely saying that all methods were regarded as inferior to that in which the ends of the vessel are brought together by an everting type of suture, the stitches passing through the entire thickness of the arterial wall. This continuous, everting mattress suture of silk, which brings intima to intima and turns the ends of the vessel outward, is quite reliable. I am quite sure that this is superior to the method Crafoord subsequently adopted for humans, in which he attempts to get an anatomical repair by abutting together intima to intima, media to media, and adventitia to adventitia. In our hands, such anatomical repairs were far inferior to the results which could be obtained by the type of anastomosis which I have described above.

Crafoord, of Sweden, was the first to repair a coarctation of the aorta in a human. The general approach we have used is similar to his. The type of anastomosis is quite different. The approach must be through the back, as one is dealing with a lesion that is deep in the chest, and the operative exposure must be adequate. The left lung is temporarily collapsed during the operative procedure; it is immediately expanded at the end of operation. The first problem is to free up a segment of aorta several inches in length. This is a time-consuming job because, if hurried, an accident may result in a catastrophe. The dissection must be exceedingly slow and delicate, because only in this way is it possible to avoid disastrous mistakes. The nearby intercostal arteries must be liberated, but usually can be left intact. Tapes passed around the aorta provide handles by which the vessel can be manipulated safely

and can be pulled away from the spine, permitting a dissection and freeing of structures which lie beneath it. The ligamentum arteriosum (or a patent ductus) must now be divided. Appropriate clamps are applied above and below the narrowed aortic segment, which is now cut out.

Obviously, a complete relief of hypertension will depend upon cutting out a sufficient amount of aorta so that the remaining ends of aorta have lumina of nearly normal size. The aortic ends are brought together by the assistant, who is holding the two aortic clamps. Thus the ends of the vessel are approximated and no tension comes on the stitches while the surgeon is inserting them. When the anastomosis is completed, the aortic clamps are removed. In the vast majority of cases, there is no leakage from the line of suture. In the occasional case, there will be one or two pinhole-size openings which require an extra stitch or two for their closure.

One of the problems of aorta surgery is concerned with the fact that some humans have a very long zone of constriction, the complete removal of which leaves a long gap, and it is impossible to bring the remaining ends of the vessel together. To overcome this difficulty, we have had little success in turning down the left subclavian artery and anastomosing it to the distal aorta, as has been suggested by Blalock and Parke; in my hands this method has been disappointing in the relief of hypertension. I prefer to deal with these situations by the insertion of an aortic graft. Extensive laboratory observations show that a high degree of success attends the transfer of a segment of aorta from one dog to another. Such grafts have been left in place for as long as two years. We have developed methods whereby sterile pieces of aorta can be obtained from suitable human autopsies, can be kept in a nutrient medium at 3–4 C. for four or five weeks, and are thus available if needed for insertion in a subject who is left with an aortic gap following removal of a long aortic segment.

I have placed twelve human aortic grafts into humans for overcoming a gap created by excision of a long coarcted segment. Two of these patients died five days later from

renal disease, the other ten have been alive for periods varying up to two years. All have maintained an excellent aortic pathway, and have had amazing relief from their previously existing hypertension. We can make no predictions about the long-term results in these cases, but to date the clinical course of every surviving patient is extremely satisfactory.

The results of surgery for treatment of coarctation are now available for analysis, and I would like to summarize what has happened in the 130 cases that I have personally operated upon. The youngest patient was 4 years and the oldest 38 years. Twenty-four patients were below 10 years of age, 63 were in the range from 10 to 20 years, 35 were 20 to 30 years, and 8 were over 30 years of age. In the early part of this work there were 12 patients who presented findings during thoracic exploration which made me decide to withdraw from the chest. Most of these were instances of very long segments of constriction for which there was little chance of instituting effective therapy. Today, when grafts are available, such conditions can be treated, and it is rare to have operations which result only in exploration. Of the remaining 118 cases, wherein a coarctation was removed, there were 12 deaths, leaving 106 who have survived. Five of these fatalities were types of deaths which probably will always be associated with this type of surgery—hemorrhage, cardiac arrest, et cetera. The other 7 were deaths due to circumstances which can largely be avoided by better selection of operative material such as refusal to operate upon patients with associated aortic valvular insufficiency, severe mitral (rheumatic) stenosis, and serious conduction-bundle defects. With a more careful screening of cases for surgery, the operative mortality can probably be reduced to 5 or 6 per cent. Indeed, in our last 50 cases there have been but 2 deaths.

Of the 106 subjects who have survived operative removal of a coarctation, the results are as follows. One had no relief of hypertension, a fact which was predicted before surgical closure of the chest because it was impossible to get a satisfactory anastomosis (a number of poorly placed stitches so compressed the anastomatic area that the lumen was prac-

tically shut off, and the aortic obstruction still exists). Eight obtained fairly satisfactory relief from hypertension, by which is meant that arm pressures which were 190 to 200 mm. of mercury systolic prior to operation have dropped to 160 or 170. Technical difficulties at the operating table were such that it was impossible to establish an aortic pathway of full size. These eight subjects have been relieved but cannot be classed as cured. In the remaining 97 patients there has been complete relief of hypertension, by which we mean that the arm pressures of adults are less than 140 mm. of mercury, and that children have pressures which are lower than this and are normal for their respective ages. The reduction of pressure occurs to some degree within 24–26 hours after operation and indeed in a few patients it is complete in this time. It is more customary, however, to find that it requires one or two weeks to dilate the arterial bed in the lower part of the body and that concurrent with this the arm pressures will fall to satisfactory levels. It is highly important to emphasize that it is not sufficient merely to excise the *narrowest* part of a coarctation; such an incomplete operation will result in living patients but they will have incomplete relief of the hypertension. To state the problem another way, the surgeon must remove *all* of the narrowed aorta and establish a pathway of normal or nearly normal size if any consistent results in complete relief of hypertension are desired. To remove all of the narrowed area is frequently an exceedingly difficult task, but the goal must be constantly borne in mind if one is aiming for superior postoperative results.

It is well to add a word about the ages at which these operations can be done. We do not like to perform this type of surgery before the age of eight or ten years. While it is technically possible to remove a block in a small child, and to give him a pathway normal for his age, we do not know for certain that the area of anastomosis will grow sufficiently as the subject develops during the next decade or more. Therefore, I have felt that it is better to defer operation (when possible) until subjects are at least eight or ten years of age, so that the anastomosis will be sufficient during the adult years.

On the upper end of the age scale there are some deterring factors having to do with degenerative changes in the aorta. While I once feared that such secondary changes would make this surgery useless or impossible in adults, our surgical experience now shows that this is not so, particularly since grafts are available to care for the more difficult types of cases wherein the aorta has little elasticity. It is well to bear in mind, however, that when dealing with older candidates for surgery, particular attention should be paid to the myocardial reserve and to the adequacy of the conduction system. With such precautions, we can avoid extremely risky operations on subjects who would probably succumb during surgery but who probably could eke out a few more years if not operated upon. Our observations to date indicate that the surgeon has his best chances of performing aortic resection in subjects from 10 to 30 years of age, but these limits are by no means fixed ones.

In conclusion, permit me to express my appreciation for the opportunity of meeting with you and discussing a subject of cardiovascular interest. In so short a time I have not been able to list all the details about the recognition of this congenital abnormality and its surgical treatment. The two most important things that I have learned are: First, coarctation of the aorta can be recognized very quickly and accurately by any physician who will look for it; it does not require prolonged or expensive investigation to detect this malformation. Second, the surgical attack on this problem is now on a sound footing and it carries a relatively low operative risk; there is ample evidence to show that complete removal of an aortic block will almost certainly be followed by cure of the hypertension.

PRESIDENT DEWIS—Thank you very much, Dr. Gross, for a very excellent presentation of what we all consider a most interesting subject. Discussion of this very excellent and comprehensive paper will be opened by Dr. Laurence Miscall, Visiting Surgeon to Bellevue Hospital, in New York.

Both in army and civilian life, Dr. Miscall has done an extensive amount of cardiac and large blood vessel surgery.

In the European Theatre of Operations he was consultant in thoracic surgery for one of the large hospital centers in England and later became one of the surgical consultants for the entire theatre. He is now consultant in chest surgery for the Veterans Administration. We have reason to hope that he will include in his remarks a review of the present status of cardiac and cardiovascular surgery in general. May I introduce Dr. Miscall.

DR. MISCALL—I think when one stands on a platform and hears himself introduced as having done an extensive amount of cardiovascular surgery, and then sees a display such as we have just witnessed, it is embarrassing.

When your secretary asked me to discuss a paper before this meeting, my affirmative reply stemmed partly from ignorance. I did not know that Dr. Gross was talking about aortic coarctation. When I discovered this, I seriously questioned the advisability and propriety of my appearance, and hastily suggested the name of the most qualified individual I know to carry on such a discussion. Since compliance with this recommendation would have required that Dr. Gross discuss his own paper, I accepted with the suggestion that a brief but only partial review of the present status of cardiovascular surgery would be a suitable though perhaps a poor substitute.

Until recently this field of endeavor was labeled by many as purely experimental surgery which provided little more than an outlet for theoretical, dreaming, and perhaps confused surgeons; or, a fertile field and open target for the antivivisectionists. Many had little confidence in the basic work which had been reported over the years and no faith that at some later date it would benefit patients. It is clear that such attitudes were born of ignorance for now it is evident that all this work is the foundation of the surgical accomplishments of today.

Real progress has a fairly recent origin. Brauer in 1902 advocated anterior chest wall resection for chronic constricted pericarditis, a progressive and disabling entity. Although Delorme had suggested the use of pericardial resection in 1898, it was 1920 and 1925 before its successful use was re-

ported by Rehn and Sauerbruch. Their favorable results were substantiated in the experience of Churchill and White, Blalock and Bunnell, Berch and others.

In 1939, Stewart and Heuer collected 135 cases in which pericardectomy had cured 37 per cent and improved 23 per cent of patients, with a mortality of 40 per cent. The addition of their seven cases, subsequently increased, with no mortality and all patients at least improved if not cured, attracted attention but aroused few to the possibilities of cardiac surgery. The forecast that better diagnosis, case selection, and so forth would improve results has been verified by the general acceptance of this procedure. I might say that in large tuberculosis hospitals now we have even expanded this and recently with the protective effect of streptomycin we have operated on a few patients for pericarditis rather than permit them to go on to the end stage of constricting disease.

Even after this experience, the way still remained a bit dark. Essential hypertension or hypertensive cardiovascular disease remained a purely medical problem until only a few years back when it was discovered that surgery had at least something to offer. The early and relatively restricted sympathetic resections of Peet, Adson, and Allen gradually gave way to the more imposing operations of Smithwick and like-minded surgeons. Now we can find many ready supporters of so-called total sympathectomy. All surgeons in employing such methods have been confronted with the statement that the disease was not altered; that symptoms were being treated. Most surgeons accepted this mild endorsement of admitted palliative effects until the present time when adequate follow-up at least arouses a suspicion that the progress of the disease may be altered favorably.

Still the veil of pessimism did not rise. This remained so until 1939, when evidence came to light that others had been thinking about surgery in cardiac disease, and particularly that generally neglected catch-all, the congenital cardiac. Out of Boston came the report of the first surgical success in the treatment of patent ductus arteriosus. In the past decade this brilliant piece of work by Dr. Gross has been established

as the only definitive treatment. When such defects of nature can be completely remedied with the negligible mortality of experienced hands, no more papers by anyone are required to justify surgery. Touroff and Veseil successfully applied the procedure to the patent ductus arteriosus with endocarditis and subsequently the number of such cases has grown. This epochal work accomplished much more than the eradication of a serious cause of illness. It cleared away the debris of skepticism which clouded the vision of what cardiac surgery had to offer. Some points still are argued but this cannot detract from the great impetus it has given to all surgery in this field.

The broadside from this discovery had hardly quieted down by 1945 when a second charge was set off in the form of successful resection of aortic coarctation which was almost simultaneously reported by Dr. Gross and Dr. Crafoord. Another malady had succumbed to the drive of years of study and work.

My limited personal experience does not permit me to comment on Dr. Gross' remarks. I would, however, bring out one point. Dr. Gross, in all of his publications concerning cardiac surgery has emphasized first the necessity before this work is undertaken of pursuing technical perfection in a laboratory. I certainly agree with that advice. Furthermore, after one has perfected a technic of doing the various procedures in the laboratory, one should not be surprised to find that new and trying difficulties may be encountered which were never envisioned previous to applying the procedures to a human being. This is the type of surgery which can cure gravely ill patients, but I can assure you it is long, tedious work which also takes its toll through the coronaries of the operator.

The year 1948 saw Blalock, and then Potts, meet the challenge of disease of the heart with cyanosis by the surgical construction of a patent ductus in patients with the tetrology of Fallot. It is certain that this type of surgery, which adds a new defect to those already present, does not hold the promise of the previous procedures reported. They, never-

theless, are brilliant additions to the surgical endeavors and can be finally evaluated only with the passage of time.

Many years of thought concerning disordered circulation of the heart seem to have come to fruition recently, particularly in the work of Dr. Beck. After prolonged and most tedious effort, in the face of repeated failure, he and his associates, and others stimulated by him, apparently have proved finally that the heart can be revascularized. Undaunted by the failure of grafts to augment intercoronary circulation, this work has terminated in the ability to open new channels in the heart by connecting the coronary sinus to the aorta through vein grafts. His very recent reports of the successful utilization of these methods in humans is a fittingly brilliant culmination of years of perserverance. When the possibilities of these procedures are correlated with the approach of Fauteux through sympathetic denervation and coronary ligation, one can vision the disappearance of one more frontier in the not too distant future.

Very recent times have witnessed the rallying of forces for the attack on valvular heart disease. It is far too early to make any forecast, and it is sufficient to state that at one recent national meeting two series of cases were reported, one by Bailey and one by Harken, in which success had been attained in valvulotomy or valvulectomy. In addition, I think probably all of you are acquainted with the work of Dr. Sweet in which he decompresses the circulation by anastomosis of the pulmonary vein to the azygos system.

I have not mentioned many of the other cardiac defects amenable to surgery, since time does not permit. It would be lax, however, to fail to mention the very significant additions now being made by the cardiorespiratory physiologists. Richards, Cournand, Riley, Baldwin, Wright, and a host of workers are daily carrying on experiments in cardiorespiratory physiology which are certainly improving our methods of diagnosis and treatment. This is the essence of good surgery, for accurate knowledge in the preoperative stage is the only sound approach and accurate measure of success. Yet, all of this new work goes by the board too frequently. It is a difficult thing to

convince some medical men that surgery has something to offer these patients. When Dr. Gross can collect 115 cases in Boston, I am sure there are many, many more cases around the country. If doctors would become—and particularly that section of the profession concerned in this work—acquainted with the true possibilities of this type of surgery, the future would be much more brilliant.

I am certain that as long as we have bold surgical thinkers such as Dr. Gross, Dr. Beck, and Dr. Blalock, whose thoughts are conditioned by a thorough appreciation of pathologic states and physiologic principles, the future of cardiac surgery will continue to thrive even more handsomely than at the present time. It has been my privilege to be here to talk to you, but a greater privilege to listen to Dr. Gross again.

PRESIDENT DEWIS—Thank you, Dr. Miscall. There must be some questions that members would like to ask Dr. Gross and Dr. Miscall, and I am sure they would be very pleased to answer.

DR. EDWARD A. KEENLEYSIDE—In view of the thin aortic wall below the obstruction and the lack of elasticity, I should like to ask Dr. Gross if he would hazard an opinion as to the possibility of an aneurysm developing.

DR. GROSS—I am not so much worried about an aneurysm developing at a later date because of the thinness of the wall beyond an anastomosis. It has been shown repeatedly in various laboratories that a segment of vein can be implanted into an arterial pathway and that in time the vein (which is now subjected to a higher pressure and to a pulsating type of flow) will thicken up and become almost like an artery. Hence, in a human, where there is this problem of a thin vessel below an aortic anastomosis I would predict that the thin vessel below will probably thicken during subsequent months and years.

DR. RAYMOND C. SCANNELL—I should like to ask you this, Dr. Gross, is the culture of a bit of the aortic graft used as an index that the graft is in suitable state for use? What is the concept of the function of the graft? Is it to provide a

stroma in the form of the elastic fibers of the medial part of the wall, such as grafts of bone? Or is it the function of the graft to provide cellular elements which will live and survive in the host?

DR. GROSS—I think this could lead to a very long, theoretical discussion, which I will try to condense. When we first started out with the graft work, we had the feeling that our best chances of success would come if we could put in a viable vessel. But, to be perfectly frank, I am now not so sure that a graft has to be viable. We have purposely killed vessels in many different ways, and have shown that they can be implanted into a recipient animal with a fair degree of success. Some of these fail, but the fact is that many survive. Therefore the graft cannot be providing living cells; it must be acting merely as a strut or scaffold along which the host builds a new vessel.

Over a period of time two things develop from the host. First, the intima will grow in from the host vessel and will cover the interior of the graft. Second, the host will lay down a new adventitia. We take great care in implanting our grafts in some sort of a bed, to take advantage of this propensity of the host to make a new outer coat. The end result is a graft which has merely been a framework, along which the recipient animal or human makes a new vessel.

Now, if this whole concept is true, it might not be necessary to put in viable vessels, but it is my feeling from experimental observations that living grafts give, on the whole, results which are a little superior to those which are obtained when dead grafts are employed. In our work on humans, only viable vessels have been employed.

I might add one more thing. We have not been worried about human grafts producing aneurysms. Our experimental studies show that a host forms such a thick and completely encircling adventitial coat that aneurysmal dilatation seems to be a very insignificant problem.

PRESIDENT DEWIS—Are there other questions? If not, thank you very much, Dr. Gross and Dr. Miscall.

We are fortunate to have with us Dr. O. H. Perry Pepper, Professor of Medicine at the University of Pennsylvania Medical School.

Those of us from the East will require little introduction to Dr. Pepper. He has had a most distinguished medical career, as is shown especially by the fact that he is Past President of the American College of Physicians and of the Association of American Physicians. He is currently Chairman of the National Research Council's Committee on Medical Problems of Veterans. I think we will find his message on "Medical Follow-up Studies of Veterans," of considerable interest. I am happy to present Dr. Pepper.

# MEDICAL FOLLOW-UP STUDIES OF VETERANS

O. H. Perry Pepper, M. D.

*Professor of Medicine*

*University of Pennsylvania School of Medicine*

*Philadelphia, Pennsylvania*

First, I want to thank you for this opportunity to present to you a chance to cooperate with the National Research Council of the National Academy of Sciences in an effort to advance the knowledge of medicine and specifically to help the Veterans Administration care for our sick and wounded veterans.

Advance in medical knowledge comes about in a number of different ways. Sometimes from a single observation or a single case properly appreciated by an alert physician—the fortunate possessor of the prepared mind. Sometimes a new discovery comes by what appears to be a sheer accident. There are several such recorded in medical history and a recent incident is another. An antihistaminic drug for the relief of allergic conditions was sent for trial to the Johns Hopkins Hospital. It was given to a patient with chronic hives which had resisted all treatment. A month later the patient reported that the hives were no better but that since the tablets had been taken, she was relieved of a life-long motion-sickness even in trains and automobiles. This drug is now widely and successfully used for the avoidance of seasickness and airsickness. This is an example of what has been named serendipity after the three princes of the Indian kingdom of Serendip. They were sent out in the world by their father, each to seek a certain object. Each returned having failed in his search but having discovered something else.

Sometimes advances in medicine are achieved by the intensive investigation which we term research, a word which means no more than search and search again. As a rule, successful research depends upon some new methodology.

A new method opens up new avenues of research and leads to advance of the horizon of medical science. Often this research is carried out in the laboratory, but progress has also been made at the bedside and in the record room. Clinical syndromes have thus been recognized and established to the great advance of medicine. It is only from the study of groups of cases of a given condition that the results of treatment can be evaluated. Similarly, the life history of the disease is learned only by prolonged observation of many patients suffering from a given condition.

One of the difficulties which is inherent in this type of clinical research is that in the usual civil practice of medicine, no sufficiently large number of cases of any certain condition are seen by one physician or even by a single hospital group. This difficulty has led to many cooperative efforts but even these have often failed to gather sufficient data when the disease in question was even relatively rare. Unless a considerable number of patients and records can be gathered, the statistical results cannot be accepted as valid, and it is of the utmost importance that a very high percentage of the patients of a given group be followed up to make the results of the study conclusive.

After World War I, it was realized that the Army and Navy records and the returning veterans offered a wonderful field for mass statistical follow-up study. Plans were made but, unfortunately, little was accomplished—the opportunity was lost.

The same chance is presented by World War II, and an even better chance because the military records are far better and the Veterans Administration's medical department is in a far healthier condition. Also, the number of patients during the war was greater and the number of those in veterans' hospitals, or with claims upon the Veterans Administration for pension, etc., is enormous. Also, the World War II patients offer unique material for study of the diseases acquired in the campaigns in the Pacific islands, in Burma and elsewhere.

Obviously, this opportunity to study by careful follow-up a great variety of diseases and their results, as well as the end results of various therapeutic and surgical procedure, should not again be allowed to slip through our fingers.

No new methodology was required except to the extent that the follow-up program should deal with larger numbers and be more carefully planned and executed. The large numbers of patients involved offered a greater source of information, but at the same time made the carrying out of a satisfactory follow-up review more difficult. In some of the groups to be studied, it is necessary to continue the follow-up for many years until the death of the patient.

We need not discuss the advantages that will accrue to the individual veteran, for it is obvious that not only the new knowledge learned may benefit him, but also he may often be helped by what is learned about him individually at the time of the examination. Thus, for example, a nonhospitalized veteran is examined for the purposes of the follow-up and it is discovered that he has a recurrence of his malaria or amebic dysentery, or that another who has had a gunshot wound of his brain has developed epilepsy.

During World War II, about 14,500,000 men, or 20 per cent of our male population, were medically screened and cared for to the full limit of need. As a result there was created a set of medical records which constitute an unparalleled fund of information on the medical, surgical, and psychiatric status of an enormous segment of our male population in the productive age groups. Early in 1946 the Surgeon General of the Army called attention to this fact and pointed out further that enlightened records-management policies in the armed forces, coupled with the fact of veteran status, created the opportunity for a research program of medical follow-up studies which could not be neglected.

Following a conference of widely representative medical interests, and a technical study by a committee of the Division of Medical Sciences, National Research Council, the Chief Medical Director of the Veterans Administration requested

that the Council form the present Committee on Veterans Medical Problems to organize and direct a program of medical follow-up studies. This step was taken with the approval of the Surgeons General of the Army, Navy, and Public Health Service. Financial support was assured by the Veterans Administration, and access to military records granted by the military agencies. The program has thus become a cooperative one among the armed forces, the Veterans Administration, and the National Research Council.

As many of you know, the National Academy of Sciences is not a federal agency but was established by an act of Congress in 1863 to advise the federal government on scientific and technical matters. It is a learned society functioning through its principal operating component, the National Research Council. The Council is divided into Divisions, the largest of which is that of the Medical Sciences. The Committee on Veterans Medical Problems, for which I am speaking today, is the second largest activity of that Division.

During its three years of operation, the Committee has greatly increased the scope of its activities by assuming a broad advisory function to the Veterans Administration with respect to its medical research, but the medical follow-up studies continue to be a major interest of the Committee and its only operating responsibility. Many problems in medicine, notably those concerned with prognosis and the natural history of disease, can be approached only by thoroughgoing follow-up investigation. This field of clinical medicine has in the past been comparatively neglected, partly at least because efficient, unbiased follow-up requires resources over which the individual investigator rarely has mastery, and perhaps also because of the large statistical component necessarily inherent in the task. As an integral part of the Division of Medical Sciences, the Committee is free to call upon the well-known medical advisory committees which also function under the Division. These are the committees which proved so helpful during the war.

Our Committee divides its follow-up studies roughly into two types: record follow-up studies and clinical follow-up

studies, the distinction lying wholly in the fact that the clinical studies require the presence of the patient. The record studies utilize records created by others, supplemented by questionnaires and tracing techniques. It is the record follow-up studies which are the subject of this report, but some mention of the clinical follow-up studies should be made. The Committee has sponsored 20 cooperative studies in which the strictly medical parts of the work are being performed in university hospitals under Veterans Administration research contracts, with the record and statistical work being done by the Committee's own staff of some 50 individuals or in Veterans Administration hospitals with the statistical work being done by the Veterans Administration. Representative rosters are furnished by the armed forces; veterans are located by the Veterans Administration and other cooperating agencies; and the statistical staff of the Committee undertakes to plan with the medical investigator the means of recording necessary observations, to construct codes for later statistical work, and to analyze and interpret the findings from the statistical point of view. Follow-up centers have been organized to study such subjects as: psychoneurosis, peripheral nerve injury, arterial injury and the repair of arterio-venous aneurysms and fistulas, schistosomiasis, schizophrenia, tuberculosis, infectious hepatitis, fractures of the carpal scaphoid, neurocirculatory asthenia, wounds of the hand, sarcoidosis, tumors of the testis, and rheumatic fever. Our only unsolved problem in this phase of our work is how to obtain participation by the veterans. This is comparatively good under the voluntary methods we employ, but not to the level of near-completeness which of course is our objective.

The record follow-up studies are designed to take advantage of information already accumulated for other purposes by bringing it to a focus and rounding it out by means of questionnaires and tracing procedures. A problem such as evaluating methods of surgical management of peripheral nerve injuries, and of assessing the relative importance of the various determinants of nerve regeneration, is obviously not to be approached with these tools. But where a problem is posed in terms of differentials in mortality, in frequency of

hospitalization, or in disability, the Committee considers that record follow-up is the method of choice. We believe that such studies are very similar in concept to the medico-actuarial studies made by life insurance companies for their own immediate purposes, particularly the companies insuring substandard risks.

As a start we decided, early in 1948, to embark upon certain pilot studies. It was considered that the pilot study was essentially a methodological endeavor, and rosters were picked for study more on this basis than for their inherent medical interest. At the outset we decided to limit ourselves to white males, and all rosters were chosen on that basis. They include Hodgkin's disease, diabetes mellitus, duodenal ulcer, scarlet fever, syphilis, and a control group. The size of these pilot rosters varies from 174 to 629 men.

Work was begun on a seventh roster consisting of radiologists and radiologic technicians in Army hospitals during World War I, but the difficulties of identifying World War I veterans were such that this roster was temporarily set aside in favor of the syphilis roster. The Hodgkin's disease roster consists of cases diagnosed on the basis of histological study. The rosters for diabetes mellitus, duodenal ulcer, and scarlet fever are representative cases so diagnosed in the Army in 1944. No review was made of the diagnosis. The World War I syphilis roster was chosen largely to explore the difficulties of the earlier material, and to establish a lower limit upon our ability to follow World War II cases for many years into the future. Work with this roster has been far more successful than anticipated by our operations group. From the results we have obtained, we would willingly add other World War I rosters but only for a few conditions of such nature that the Veterans Administration would be expected to maintain close contact in a very high proportion of cases.

It should also be mentioned that most questions we expect to investigate require that we deal with a set of cases representing the average diagnostic ability of the medical profession as a whole, and accordingly we will not often find it desirable to institute a routine review of diagnoses made in

military hospitals. Review of samples will often seem important and in a few instances we would, as in Hodgkin's disease, choose cases only on the basis of rigorous diagnostic criteria.

For positive identification of individuals in tracing for mortality, we have routinely employed such items as name, Army serial number, prior address, date of birth, and place of birth, as well as the diagnosis itself where appropriate. We believe that we very rarely end up with the wrong man. The tracing techniques essential for mortality studies also provide the basis for any direct queries of the men in connection with hospitalization and disability.

The numerous files of the Veterans Administration provide the best single source of information on the whereabouts of individuals on our rosters, particularly files of death cases, of hospitalizations, of disability claims, and of insurance. Over 98 per cent of the 2,755 men in these pilot rosters were known to the Veterans Administration, although in many cases the Veterans Administration did not have information as late as our cut-off date, 30 June 1948. That the relation between the Veterans Administration and the veteran population is not one of automatically and rapidly decreasing contact you know from the fact that about 65 per cent of Veterans Administration beds are filled by men receiving care for non-service-connected complaints, and from such events as bonus payments made many years after World War I, and the insurance dividends distributed by National Service Life Insurance. Arrangements were made with several other federal agencies to search their extensive files for evidence that men on our rosters were alive or dead. Applications for bonus certificates, for terminal leave bonds, and the like, were searched. When these methods failed we employed the Retail Credit Company and also had one search made of the files of the credit bureaus. Since the latter agencies could not assure positive identification by their indirect methods, mail inquiries were made at the addresses they furnished. By these means we were able, by 1 June of 1949, to trace all but about 200 of our 2,800 men to our cut-off date of 30 June 1948. At that time we solicited

the aid of about 20 of the largest life insurance companies to see whether life insurance files would be effective in tracing our difficult cases. The cooperative spirit with which our requests have been received by the individual companies, and the interest shown in the problem by the Medical Section of the American Life Convention, have been most encouraging to us. Moreover, the search of insurance files was, in our opinion, a rewarding one. Twenty-four per cent of our problem cases were found to have insurance records, and more than two-thirds of these had insurance records sufficiently up to date to enable us to complete our search. Although in this instance our identification techniques were reasonably good, we extended them by means of direct mail contacts with the veterans so located. We are very grateful for the aid which the life insurance companies have given and may continue to give.

With the aid of the American Red Cross, and by dint of checking every lead furnished us, we have now been able to reduce our untraced group to 81 men, 2.9 per cent of the number under study. Of these, 43 are World War I veterans, and the percentages traced are 90.8 for World War I and 98.5 for World War II veterans. We shall keep after the 81 men and believe that a substantial portion of them will be found in time.

If, for the World War I cases, we drop back only 15 months to a cut-off date of 31 March 1947, our percentage loss drops from 9.2 to 4.7. At the twenty-year mark it is 2.8, and at the ten it is 1.9. We think of these figures as an upper limit on our losses with World War II cases, and in planning a long-range program we are heartened by this result, undertaken 30 years after the fact and on material which we consider much more difficult to work with than the World War II rosters. Another encouraging sign to us has been the finding that 98.8 per cent of all the observed deaths on our rosters are known to the Veterans Administration. Of these deaths which occurred after return to civilian life, 98.2 per cent are known to the Veterans Administration. We know, there-

fore, that the bulk of our mortality information can be obtained from the Veterans Administration.

Because we are interested in all of the hospital experience of a group of veterans since separation from service, we are not content to extract data only on hospitalization in Veterans Administration installations, but we go directly to the man with a simple questionnaire about his health and hospital experience. At this point we have already located him in connection with our tracing for mortality, or we have an address to be used in verifying identity. Since we know the Veterans Administration portion, whether he responds or not, we are in a good position to test whether those who fail to respond have a different rate of Veterans Administration hospitalization. Similarly we have a good notion of the accuracy of questionnaires by comparing the Veterans Administration hospitalizations they report with official Veterans Administration records. The one missing piece is the non-Veterans Administration hospitalization of non-respondents.

Questionnaires and letters have been used. Although we do not yet know how responsive a group will be on repeat inquiry, say after two years, we are encouraged by the fact that thus far 82 per cent of the 2,350 men not known to have died have returned questionnaires. If we omit the 198 men for whom we do not yet have a correct address (81 untraced and 117 known to be alive but not yet accurately located), the figure is 83 per cent for World War I and 90 per cent for World War II veterans. Moreover, we have seen exceedingly little evidence of hostility in the material returned, and we are hopeful that we can keep in touch with our groups by this means.

The missing portion, non-Veterans Administration hospitalization on the part of non-respondents, amounts to an estimated 10 per cent of all hospitalizations. We have elected to sample this group and have been exceedingly fortunate in obtaining the assistance of the Red Cross in making a direct inquiry along the lines of our questionnaire and in recording the result on the attached form. The non-respondents in-

clude men whom we have not successfully located as yet, but the indications are that the Red Cross will return schedules on a very high percentage of those who are definitely located, and on perhaps 50 per cent or more of the total. Thus, although we cannot expect 100 per cent coverage for non-Veterans Administration hospitalization, we shall have a great deal of information upon which to base careful estimates for an entire roster.

Cause and duration of hospitalization we know quite accurately from Veterans Administration hospitalization records. For non-Veterans Administration hospitalizations the information is much less accurate, but again we have a basis for understanding its shortcomings by comparing questionnaire data on Veterans Administration hospitalizations with official Veterans Administration records.

Of the three areas of interest in these studies, disability is perhaps the least important to us at present. This phase is much more elusive, and of course Veterans Administration disability ratings were never intended for scientific purposes. However, they represent information which can be obtained at little additional cost beyond that necessary to secure mortality and hospitalization data, and we have felt obligated to gather it and to see what we could make of it. Moreover, we are in a position to learn how well disability ratings compare with independent evaluations made in university hospitals in connection with our clinical follow-up studies. Comparisons of this sort will probably determine the future of our disability studies.

On our questionnaire we have included very limited questions about occupation and ability to work, expecting that this information will provide a useful supplement to the Veterans Administration data.

It is too early to make any statements about any scientific results. Only preliminary tabulations have been made on data collected under the program, and these were made quite some time ago. In a few months hence we expect to have an adequate analysis of the data, not merely from the stand-

point of method as discussed above, but also from the standpoint of comparisons of interest to medical science. We already have an approximate table of survivors of Hodgkin's disease. Arrangements have been made with the Armed Forces Institute of Pathology to prepare a joint report in which pathologic determinants of end results would be evaluated. We hope to add Navy cases to our roster in this study.

Our future plans can be briefly stated. The record follow-up studies have been made a permanent part of the Committee's program, and it is expected that more rosters will be added slowly, and only after careful study by advisory groups in the fields of major interest. The size of the program has not been fixed, but we would expect to be able to follow perhaps 25,000 to 50,000 men. Rosters will be no larger than seems required for significant results by statistical standards, so that we may cover as wide a medical field as possible. We hope that repeat follow-ups will be necessary no more often than every two years, and that as the program matures we shall be able to make increasingly accurate corrections for bias in response.

It has already been clearly demonstrated that life insurance companies can make a definite contribution to these clinical follow-up studies by giving aid in the tracing of the relatively small group of men not found by other means. The group which we have referred to some of the larger companies not only comprised the men we had found most difficult to trace, but consisted in considerable degree of men who would be expected to buy little if any commercial life insurance, because they have already given up or never took out National Service Life Insurance and because many of them are "floaters" who leave no forwarding addresses, do not establish credit records, and the like. The Committee is grateful for assistance thus far, and hopes that the program may be of sufficient interest to the life insurance companies to warrant continued cooperation along the same lines. We believe that we can hold the volume of our inquiries to a level which will not seem burdensome, particularly if we are successful in staggering the load over a period of years. Our expectation is that we could

hold the volume of our requests to a list of 1,000 names each year. Our method thus far has been to circulate the same list simultaneously to each of the larger companies, and it would seem that a scheme could be devised whereby more use was made of companies with essentially local coverage and whereby successive companies would not be asked about cases already identified by companies making an earlier review of the list. It is our earnest hope that the life insurance companies will participate in the program, and that ways will be suggested whereby the effort required of them will be minimal.

We believe the objectives of these follow-up studies are well worthy of your support—they may prove to be of real scientific value, of benefit to the veterans—and that the data gathered may be of value to the life insurance companies themselves.

PRESIDENT DEWIS—Thank you very much, Dr. Pepper. Perhaps someone has a question to ask either Dr. Pepper or his associate, Dr. Beebe, who is present at this meeting. Doctor, is it true that you have some mimeographed sheets for distribution? Would you like to say a word about those?

DR. PEPPER—There are some mimeographed sheets listing the membership of the committee. A list of the subjects also is given; and what else, Dr. Beebe?

DR. GILBERT W. BEEBE—Follow-up tracings are included. Results are there too, in brief form.

DR. PEPPER—By one insurance company?

DR. BEEBE—These are by all insurance companies together.

DR. PEPPER—Thank you, gentlemen, for listening to me.

PRESIDENT DEWIS—Thank you very much, Dr. Pepper. Our next paper is entitled "The Disease Called Arterial Hypertension—The Newer Ideas," by Dr. Cecil C. Birchard, Chief Medical Officer of the Sun Life Assurance Company of Canada.

Dr. Birchard needs no introduction to this audience as he has been a member of this Association for almost twenty

years. He is not only chief medical officer of a large Canadian life insurance company but also a cardiologist of considerable distinction. We will now have the pleasure of hearing Dr. Birchard's paper.

# THE DISEASE CALLED ARTERIAL HYPERTENSION

CECIL C. BIRCHARD, M. D.

*Chief Medical Officer*

*Sun Life Assurance Company of Canada*

It is with considerable diffidence that one undertakes this task. Since that date in 1733 when Rev. Stephen Hales became famous by vivisecting his old gray mare and measuring her arterial systolic pressure and likewise her venous pressure, there has been continually increasing interest in blood pressure, and much effort has been expended to provide answers to a number of obvious questions.

What are the normal ranges of systolic and diastolic blood pressure in man? What are the underlying morbid processes which cause chronic disturbances?

The younger members of this Association may not be acquainted with its contributions to this subject in the past, and, if you will bear with me, I will recount these.

The activities of members of this Association, with the assistance of the Actuarial Society of America, provided a satisfactory answer to the first question above; that is, the normal ranges of systolic and diastolic blood pressures in man. Clinical medicine lacked the facilities for providing such an answer, but the well handled mortality data of the insurance companies could, and did. And likewise, the same material showed to be of grave import some previously disregarded blood pressure disturbances, a fact which clinical medicine was slow to recognize. Now, the slowness was because statistical methods were not in favor at that time, nor were they appreciated by our profession. In the teens of the present century, clinicians were loath to accept the thesis that transient elevations of blood pressure could be of adverse significance. The apology was made that the patient was nervous, and indeed at that time some very eminent clinicians

were still of the opinion that the unaided finger was a very good sphygmomanometer and that elevated blood pressure, unless extreme or corroborated by unmistakable cardiac enlargement or eyeground changes, was of no importance.

But the second obvious question, the "why" of arterial hypertension, is of a different sort, amazingly complicated, compounded of perhaps a dozen independent variables with, superadded, a large but unknown number of interrelated variables. The problem is physiologic, biochemical, and biologic, and some of the problems are biophysical. One resurgent and not too bashful branch of our profession suggests that it may be psychological. I suggest that the difficulties besetting the solution of this problem will eventually be accounted to have been more difficult than those of malignancy. With the advent of a convenient and more or loss accurate technic for recording systolic blood pressure, say fifty years ago, and later a rough method for diastolic pressure, the higher planes of clinical medicine became interested. Age, height, weight, pulse rate, and body temperature excepted, it was the first biometric measurement to be accepted as a routine clinical procedure.

Before this Association, the first papers to mention blood pressure appeared in the records of the twenty-second annual meeting, October, 1911. One paper by the late Dr. J. W. Fisher (Northwestern Mutual Life Insurance Company) reported average systolic pressures in life insurance applicants and the relative mortalities obtained in small groups observed over short periods. These were classified by systolic pressures only. Diastolic pressures were not mentioned. At the same meeting a non-statistical paper by Dr. Charles F. Martin, Professor of Medicine, McGill University, and Medical Director of the Standard Life Insurance Company, gave a clinical appraisal of systolic and diastolic blood pressures, stressing the importance of the diastolic from the standpoint of diagnosis. At that meeting, the late Dr. Oscar H. Rogers of the New York Life outlined his plans to perfect an instrument to be known as "Dr. Rogers' Simplex Sphygmomanometer." According to the description, this instrument appears to have been of mercury manometer type but rather extra-

ordinary in being arranged to have the cuff pressure force the mercury up the manometer against the elastic pressure of air imprisoned in the tube which had a hermetically sealed bulb at its upper end.

The medical profession of every continent knows a different instrument, but of aneroid type, bearing Dr. Rogers' name. That is the one sold throughout the world by the tens of thousands. The first recorded reference to the sphygmomanometer in the records of this Association appears to have been made by Dr. Edward K. Root, of the Aetna Life Insurance Company, at the sixteenth annual meeting, in October, 1905. The contributions of this Association toward the establishment of a good technic and its publication among the medical profession have been very remarkable indeed.

The earlier investigators approached the problem of temporarily and of persistently disturbed blood pressures largely on a neurologic basis. There were the vasomotor centers in the floor of the fourth ventricle, real enough, each composed of two parts, one vasoconstrictor and one vasodilator. These were alleged to be definitely separate and individually stimulatable by small electrodes. More recent investigators find evidence of other centers higher up in the hypothalamus and in the mid-brain, acting through centers of the vasomotor nervous system. Stimuli reaching these centers by afferent paths "arc", or "short circuit" to the cardioinhibitor or cardioaccelerator centers close by, and thence to efferent paths to produce pressor or depressor responses, depending on which center is involved. The "arcing", or "short circuiting" can take place at many lower levels.

Acting through, or independent of, the vasomotor paths and centers of the central nervous system are a series of reflexes collectively controlling pulse rate, changes in peripheral resistance, and the minute volume output of the heart. Among these are Marey's reflex, or the physiology by which rising aortic blood pressure exerts a measure of control over cardiac output and peripheral resistance in the arterioles; the Bainbridge reflex whereby distention of the great veins and right

auricle causes increased heart rate; and, most important, the carotid sinus with its anatomically and physiologically associated glomus caroticum, and that other small body of similar functions, the glomus aorticum—these two conspire to keep the higher centers continually well posted on the pressures within the carotid artery and aorta.

Then comes the chemical controls on the heart and blood vessels by adrenalin and its very near relative, arterenol, by carbon dioxide, lactic acid, oxygen, and by the newcomer, angiotonin. In speaking of controls thus far, for the most part one has had in mind the minute-to-minute controls of the blood pressure mechanism necessary for comfortable living and meeting emergencies. At an early date, as investigation passed from the normal to the morbid, the concept of "pressor" and "depressor" substances appeared, and for obvious reasons the kidney was immediately suspected of originating "pressor" substances. In 1898, two writers in the Scandinavian Archives of Physiology announced they had discovered a renal pressor extract in the kidney, and they believed it originated in the adrenal cortex, which was probably wrong. They gave it the now well known name of "renin"—r-e-n-i-n, not r-e-n-n-i-n—and later, observers in England, before 1911, confirmed this finding. Now renin appears persistently and frequently in the more recent literature on arterial hypertension. It is a ferment or enzyme like that which produces alcohol and therefore it is a protein and is produced by the renal tubules. It is not a pressor substance. Hans Selye, of Montreal, by obstructing renal circulation stimulates the formation of cells in the tubules morphologically resembling cortical cells of the adrenal, and accounts them a source of renin. The similarity with adrenal cells is of very considerable interest. Renin splits an alpha globulin, produced by the liver, to produce the substance angiotonin, or hypertensin. Unlike renin, it has extraordinary pressor properties. Angiotonin stands between the proteins on the one hand and the amino acids on the other, but very close to the amino acids. It is a combination of some three or four amino acids and falls into the category of the peptides.

During innumerable attempts by clinical experiments to produce a state approximating essential arterial hypertension, there was no success until comparatively recently. The first gratifying result came through the genius and good luck of Dr. Harry Goldblatt who demonstrated that clamping the renal arteries produced a persistent hyperpiesis, both systolic and diastolic, which did not disappear when the obstructions to renal blood supply were removed. Later, the application of cellophane envelopes to the kidney, with resulting sclerosis of the cortex, produced the same results. These methods have the merit of simulating clinical hypertension in that the functional efficiency of the kidney as assessed by ordinary means becomes impaired.

Renal hypertension is a fact, but how does it come about? How does the damaged kidney, if it be damaged, receive its injury? How does it affect the peripheral or arteriolar outflow and cardiac output to produce systolic and diastolic hypertension?

The nervous system appears to play no part either intrarenally or extrarenally in renal arterial hypertension. Severance of renal and cardiac nerves does not affect the production of hypertension, nor does destruction of all the sympathetic ganglia and section of the splanchnic nerves relieve or prevent the hypertension. This is one of the differences between renal hypertension and clinical hypertension. Dividing the cardiac depressor nerve in the normal animal produces an unstable hypertension, variable with cardiac output. In that respect it resembles the earlier stages of arterial hypertension and also a slight degree of arterial hypertension observed in hyperthyroidism. The same effect comes from destruction of the carotid body and glomus caroticum, prime sources of afferent stimuli to the vasodepressor center.

There is no reason to inculpate any of these structures as participants in the production or maintenance of experimental renal hypertension, and while hypertension has been produced by persistent electrical stimulation of the renal nerves by implanted electrodes, it is not permanent and in no way resembles clinical hypertension.

While the nervous system appears to have no part in the production of renal hypertension by the Goldblatt or allied technics, certain observers have worried neurotic rats into arterial hypertension. This achievement is not applicable as yet to the human disorder, and, so far as I have found, not reported in less temperamental quadrupeds.

When a search is made for an endocrine intermediary between the Goldblatt kidney and the resulting hypertension, the results point to the pituitary and adrenals, more particularly the latter. Removal of the adrenals causes renal hypertensive pressures to fall, and administration of the adrenocortical hormone, desoxycorticosterone with salt, restores the hypertension. The hormone alone, without salt, has been ineffective. Similarly, when hypertensive patients develop Addison's disease with resulting destruction of the adrenals, the pressure falls but can be restored by administering cortical hormone. Removal of the pituitary likewise causes subsidence of renal arterial hypertension and desoxycorticosterone restores it.

It has been shown that adrenalectomy causes reduction or disappearance of the alpha globulin on which renin acts to produce angiotonin. Hence the absence of angiotonin results in lowered blood pressure, or so the theory goes. Here it is of interest to note that continuous overdosage with adrenocortical hormone resulting from stimulation by a basophilic tumor of the pituitary produces the hypertension of Cushing's disease.

That sodium chloride plays a part in maintenance of blood pressure has been known for a long time. Low sodium diets have been used in the treatment of hypertension since 1905, in fashion for a while and then out. The association of low blood sodium content and low blood pressure with destructive lesions of the adrenals has been known also for a long time. More recently we have the Kempner rice diet, which is salt restriction with low protein intake and absence of fat, the energy-producing factor being rice starch. It is an abominable diet from the standpoint of palatability and otherwise, and it

is difficult to imagine that it can have any real and permanent value. When the patient abandons the diet, there appears to be a definite tendency to return to a degree of hypertension as high or higher than when the treatment began, and there is a real hazard of congestive heart failure.

During the last war, patients kept on similar low calorie, low protein, low fat diets for long periods in the concentration camps of Germany and Leningrad during the siege developed heart failure and hypertension after resuming a normal diet. Brozek, Chapman, and Keys in 1948 made similar observations in a group of young healthy males kept for a prolonged period on 1600 calorie diets. One of their subjects developed very definite congestive heart failure though perfectly healthy when the experiment was begun, when on something comparable to a prison camp diet.

That high sodium intake can predispose to vascular degeneration, nephrosclerosis, and arterial hypertension appears to be well established for chickens and possibly for mammals. Hans Selye has demonstrated such findings in chickens dosed with adrenocortical hormone, the lesions being accelerated by the administration of salt, and salt alone produced similar results but less rapidly. Dr. Louis Katz published similar results, also with chickens.

In human arterial hypertension there is not much reason to account the condition a renal hypertension comparable with the experimentally produced disease. In arterial hypertension, the renal blood flow is not obstructed until late in the disease, and the percentage terminating in death by renal failure is only of the order of 10 per cent. While obstruction of the renal flow occurring spontaneously from any of numerous causes does on occasion associate with arterial hypertension, and from time to time removal of a nonfunctioning kidney gives a remission of the associated hypertension, yet the association of obstructed renal blood flow or of a nonfunctioning kidney with arterial hypertension is only occasional and is definitely not the rule. This feature of the disease has led certain authorities to postulate intervention of the nervous

system to maintain the hypertension after the renal factor may have ceased to operate.

Of the myriads of hypertensive patients who are humbugged, consoled, and depleted of their cash, there is a small group of known causation—those who owe their high pressures to intoxication from the adrenalin and arterenol secreted by pleochromocytomata in the medullary tissues of the adrenal glands. Arterenol, more strongly pressor than adrenalin, has been demonstrated in such tumors by chromatographic analysis. The percentage incidence of these among the whole of the hypertensive population has been estimated at one-half of 1 per cent, or one in two hundred. Hitherto, this variety of hypertension has been accounted as always episodic, recurring bouts of hypertension of brief duration, the clinical manifestations being anxiety, pallor, sweating, and extrasystoles, symptoms commonly seen clinically after adrenalin medication. However, it is now recognized that such patients may have continuous hypertension on which the episodes stand like isolated mountain peaks set on a plateau.

The recognition of this feature may be expected to increase the number of cases diagnosed and appearing in the literature. The technic of diagnosis is to infuse intravenously adrenalin-destroying drugs such as benzodioxane, and observe the amount and duration of the resulting fall in the blood pressure, and also to demonstrate a hyperadrenalinemia quantitatively by bio-assay. The cat lends itself quite well to that procedure. If the tumors occupy the sites which well behaved adrenals should occupy, their removal is not too difficult and dramatic cure results. One difficulty arises from the tendency of adrenal tissue to squat in unorthodox places, with the result that adrenal tumors are not always located where they should be.

Another group of patients with arterial hypertension consists of those who have had serious streptococcic infections, and probably streptococcic bacteremia. A chance observation of years ago made it possible for one to predict the onset of arterial hypertension in three of these cases; and one of them,

still alive, has normally functioning kidneys, notwithstanding the fact that he has had the disease for over ten years and is approaching a cardiac termination.

As medical advisers of life insurance companies, we should be able to predict the group mortality rates of patients falling into various blood pressure categories. We habitually make such predictions with varying degrees of success. The statistical data on which these predictions are made are as well known to you as to me. But these group predictions are of little use when one deals with individuals. In assessing the life expectancy of the individual, provided one can get a good history, which is not usually the case with applicants for life insurance, I believe that one can make pretty good guesses of future events. The bases are elapsed time since onset of the disease and the physical condition at the time of examination, elapsed time being of prime importance.

Like animals and plants, every disease has an average life history. In arterial hypertension it is my belief that it is divisible into three five-year periods. The first exhibits only a more or less variable systolic hypertension; the second five years a higher fixed systolic and beginning elevation of the diastolic and the beginnings of the characteristic electrocardiogram of the full-blown disease, perhaps with a degree of cardiac enlargement; the third five years, definitely enlarged heart, a still higher diastolic pressure, the systolic perhaps a bit lower, the full-blown hypertensive electrocardiogram, eye-ground changes, and real physical disability; and in the early fourth five-year period, cardiac, cerebral, or renal death in that order of frequency. Having used this classification by five-year periods, one has had the satisfaction of seeing too many conform to the pattern.

From what I have said, and from the literature generally, a casual observer might conclude that the pernicious results of the disease under consideration were simply on the basis of the elevated hydrostatic pressures obtaining inside the vascular organs, and that all evil results would disappear if the pressures could be controlled. No one would claim that

there are no evils directly and solely due to the elevated pressures, but it is certainly not plausible to leave it to be inferred that the reverse is the case. This notwithstanding, we will probably have to be content with blood pressure figures as one of our better measures for assessing the benefits of treatment on a short-range basis.

Blood pressures do fall and hearts do get smaller in patients on the Kempner rice diets. They did precisely that in those subjected to similar diets in the concentration camps of Europe; and when the victims went back to normal dietary habits, the pressures went higher than before, and they developed heart failure.

In the appraisal of the results of high dorsolumbar sympathectomy, one excellent five-year follow-up, by Evelyn, Alexander, and Cooper, the results have been otherwise than good. Among the males, at the end of five years 81 per cent were unimproved or dead—36 per cent were dead. That has led some surgeons to say, "Well, these patients should have been operated on before," but, had they been operated on before I presume they would have still had five to ten years' expectation of life, and it would have taken a very long observation period to prove anything either for or against the operation.

While my comments have been the reverse of constructive, there is no criticism of those indefatigable workers who have tackled this most difficult of all medical problems. Some day we will know whether the answer is renal, adrenal, nervous, or hepatic, and whether the prime outside cause is diabetes, infection, or heredity.

PRESIDENT DEWIS—Thank you very much, Dr. Birchard.

Gentlemen, this concludes our scientific session, but before the close of the meeting I should like to express my thanks for the many courtesies you have extended to me during the past year. I particularly wish to thank the various committees for their splendid cooperation, and my very able associate and your secretary, Dr. Kirkland, for his assistance.

I now take very great pleasure in presenting your new president, Dr. Harry E. Ungerleider, the Medical Director of Research, The Equitable Life Assurance Society of the United States.

PRESIDENT UNGERLEIDER—Fellow Members of the Association: I cannot tell you how much I appreciate the high honor you have bestowed upon me in electing me president of this Association.

Among my earliest memories of these meetings is the one held by Dr. Rowley at Hartford. At that particular one I almost decided to forsake a career in life insurance medicine because I believed it was beyond my scientific abilities. It is indeed an honor to succeed to the office occupied over the years by a group of physicians of whom this Association can well be proud. With your cooperation—and I feel sure of having the cooperation of each member—the Association should continue its progress. Next year we shall attempt to equal the record of the past year under the splendid leadership of Dr. Dewis.

Although it is growing late, I should like to recognize Dr. Rowley.

DR. ROBERT L. ROWLEY—With the passing of the years, our figures change. Let no one assume that I am referring to the physical outlines or silhouettes of individual members of our Association; I refer to the figures that we use in our attempts to assign a numerical value to a risk under review. Of course, our present-day figures, derived from studies carried on both within our Association and in the field of general medicine, where new information is constantly being unfolded, enable us to perform our work more intelligently than formerly. When I compare the present-day procedures and practices in underwriting with those in vogue in the early years of my experience in this work, the contrast is indeed a striking one. We have as an Association grown bigger and stronger and we owe much to those who over the years have shared their knowledge with us. I should like to take this opportunity to express on behalf of our members present our

hearty thanks to our retiring president, Dr. Dewis, and to those who have assisted him in planning and conducting this meeting. On the subject of knowledge or wisdom, may I quote these lines which seem to me to be appropriate at this time:

"Wisdom, the source of virtue, and of fame, obtained with labour, for mankind employed, and then, when most you share it, best enjoyed."*

PRESIDENT UNGERLEIDER—Is there any other business to come before the meeting?

A motion to adjourn was made, seconded and carried, and the meeting was adjourned.

The following doctors were present at some time during the sessions:

J. W. Abbott
C. B. Ahlefeld
Joseph Altman
K. W. Anderson
R. L. Anderson
T. M. Armstrong
W. B. Aten
D. R. Auten

H. A. Bancel
G. H. Barber
N. J. Barker
C. C. Beach
J. R. Beard
E. W. Beckwith
J. E. Bee
G. W. Beebe
M. F. Bell
M. B. Bender
J. R. Biggs
C. C. Birchard
W. R. Bishop
William Bolt
E. C. Bonnett
J. T. Bowman
K. F. Brandon
A. W. Bromer
F. R. Brown
H. B. Brown
Leslie Brown
Marshall Brown
R. F. Buchan
E. R. Bush
B. F. Byrd

J. T. Cabaniss
D. M. Caldwell
E. J. Campbell
H. B. Campbell
P. E. Carlisle
J. C. Carpenter
V. S. Caviness
J. P. Chapman
P. H. Charlton
J. C. Clifford
M. H. Clifford
N. B. Cole
B. R. Comeau
H. L. Congdon
J. L. Cook
H. K. Crutcher

B. A. Dawber
H. D. Delamere
E. J. Dewees
E. G. Dewis
F. R. Dieuaide
H. W. Dingman
G. D. Dorman
L. B. Dunn

T. M. Ebers
L. B. Ellis
J. A. End

A. H. Faber
J. G. Falconer
R. K. Farnham
H. H. Fellows
R. M. Filson
R. W. Finegan
Frederick Fink

*William Whitehead, "On Nobility."

P. M. L. Forsberg
E. M. Freeland
H. M. Frost

F. I. Ganot
D. S. Garner
J. H. Geddes
J. T. Geiger
Leo Gelfand
W. M. Genthner
E. E. Getman
R. A. Goodell
George Goodkin
H. W. Goos
R. S. Gubner
J. R. Gudger
H. M. Gray
C. J. M. Grisdale
R. E. Gross

David Halbersleben
Llewellyn Hall
F. T. Hallam
G. W. Halpenny
O. E. Hanes
L. E. Hathaway, Jr.
H. L. Hauge
W. C. Hausheer
H. M. Hawkins
P. R. Hawley
O. C. Hendrix
E. V. Higgins
W. L. Hilliard
E. C. Hillman, Jr.
D. W. Hoare
J. C. Horan
E. G. Howe
T. B. Hoxie
J. L. Humphreys
J. H. Humphries
B. L. Huntington
S. W. Hurdle
J. J. Hutchinson
J. R. B. Hutchinson

A. S. Irving
J. G. Irving

A. O. Jimenis
A. E. Johann
J. W. Johnson

V. L. Karren
E. A. Keenleyside
N. R. Kelley
E. F. Kerby
C. E. Kiessling
D. G. Kilgore
R. E. King
H. B. Kirkland

W. C. Lamb
Phillips Lambkin
P. H. Langner, Jr.
L. G. LaPointe
I. C. Lawler
L. H. Lee
H. R. Leffingwell
W. R. Leute, Jr.
E. H. Lindstrom
G. W. Lougheed

H. C. McAlister
F. M. McChesney
Walsh McDermott
A. J. McGanity
F. J. McGurl
L. L. McLellan
W. J. McNamara

Charles Maertz
S. J. N. Magwood
R. W. Mann
W. S. Middleton
E. B. Milam
E. S. Mills
Laurence Miscall
J. T. Montgomery
R. C. Montgomery
J. F. Moore, Jr.
J. R. E. Morden
C. V. Mulligan

S. A. Narins
M. H. Neill
R. A. Nelson

R. E. Nicholson
E. C. Noble

A. J. Oberlander
Herbert Old
B. H. Olson
J. K. Ormrod

W. C. Page
C. B. Parker
A. E. Parks
J. M. Peck
D. S. Pepper
O. H. P. Pepper
J. C. Pierson
Cullen Pitt
J. J. Post
R. W. Pratt

E. J. Quinn

J. H. Ready
C. L. Reeder
P. V. Reinartz
W. A. Reiter
W. M. Reynolds
C. P. Rhoads
C. E. Rice
G. P. Robb
D. C. Roberts
A. J. Robinson
H. B. Rollins
F. W. Rolph
R. C. Roskelley
Gordon Ross
J. G. Ross
T. F. Ross
R. L. Rowley

R. C. Scannell
K. F. Schaefer
B. T. D. Schwarz
W. H. Scoins
R. J. Scott
R. C. Secor
A. F. Seibert
D. L. Selby

Hall Shannon
J. T. Sheridan
D. M. Shewbrooks
R. R. Simmons
A. M. Sison
A. D. Smith
W. A. Smith
Isaac Sossnitz
F. L. Springer
H. F. Starr
J. B. Steele
D. F. R. Steuart
H. M. Stewart
L. Q. Stewart
I. R. Stidger
S. J. Streight
L. G. Sykes
B. C. Syverson

L. J. Tedesco
K. J. Thomson
W. B. Thornton
Joseph Travenick, Jr.
Wallace Troup
F. D. Truax
Maurice Turcotte

H. E. Ungerleider

B. W. Vale
R. C. Voss

Murray Wagman
F. A. Waldron
K. E. Ward
R. V. Ward
C. F. Warren
R. L. Weaver

Jefferson Weed
J. H. Weidner
D. E. W. Wenstrand
S. S. Werth
C. F. S. Whitney
H. E. Wiley
J. A. Wilhelm
E. S. Williams
R. L. Willis
A. C. Wilson
C. L. Wilson
G. E. Woodford

L. S. Ylvisaker
D. E. Yochem
G. G. Young
V. H. Young

R. W. Zinkann

Also present were:

J. L. Cameron

Earl Duncanson

M. M. Gorman

E. J. Hardin
R. L. Hogg

Edward King

G. C. Kingsley

Miss A. M. Lyle

A. P. Morton

G. A. Oliver

L. N. Parker

Pearce Shepherd
O. G. Sherman
Arnold Siegel

A. E. Thyselius

P. V. Wells
J. C. Wilberding

Total attendance at all sessions, 264.

## In Memoriam

**Deceased Since Fifty-seventh Annual Meeting**

William W. Dow, M. D.
Toronto Mutual Life Insurance Company
Died February 14, 1949

W. Ewart Ferguson, M. D.
Excelsior Life Insurance Company
Died August 11, 1949

Victor J. Fingar, M. D.
The Equitable Life Assurance Society of the United States
Died January 10, 1949

Frank L. Grosvenor, M. D.
The Travelers Insurance Company
Died October 15, 1949

G. Carroll Lockard, M. D.
Maryland Life Insurance Company
Died August 7, 1949

Carleton B. McCulloch, M. D.
State Life Insurance Company
Died April 5, 1949

Samuel B. Scholz, M. D.
The Penn Mutual Life Insurance Company
Died March 4, 1949

## DECEASED MEMBERS

| | |
|---|---|
| John L. Adams, M. D. | New York, N. Y. |
| Charles D. Alton, M. D. | Hartford, Conn. |
| Malcolm O. Austin, M. D. | San Francisco, Calif. |
| Walter C. Bailey, M. D. | Boston, Mass. |
| Henry A. Baker, M. D. | Kansas City, Mo. |
| A. W. Barrows, M. D. | Hartford, Conn. |
| John T. J. Battle, M. D. | Greensboro, N. C. |
| Wesley W. Beckett, M. D. | Los Angeles, Calif. |
| Charles D. Bennett, M. D. | Newark, N. J. |
| Emmanuel P. Benoit, M. D. | Montreal, Canada |
| Charles Bernacki, M. D. | New York, N. Y. |
| Thomas W. Bickerton, M. D. | New York, N. Y. |
| Albert W. Billing, M. D. | New York, N. Y. |
| Wilton F. Blackford, M. D. | Louisville, Ky. |
| David N. Blakely, M. D. | Boston, Mass. |
| Robert J. Blanchard, M. D. | Winnipeg, Canada |
| Harold E. Bogart, M. D. | New York, N. Y. |
| William M. Bradshaw, M. D. | New York, N. Y. |
| Frederick G. Brathwaite, M. D. | New York, N. Y. |
| William R. Bross, M. D. | New York, N. Y. |
| Chauncey R. Burr, M. D. | New York, N. Y. |
| Robert L. Burrage, M. D. | Newark, N. J. |
| James Campbell, M. D. | Hartford, Conn. |
| Frank H. Carber, M. D. | New York, N. Y. |
| Willard B. Carpenter, M. D. | Columbus, Ohio |
| Frank W. Chapin, M. D. | New York, N. Y. |
| Frederick W. Chapin, M. D. | Springfield, Mass. |
| Ferdinand E. Chatard, M. D. | Baltimore, Md. |
| Charles L. Christiernin, M. D. | New York, N. Y. |
| Henry Colt, M. D. | Pittsfield, Mass. |
| Herschel F. Connally, Sr., M. D. | Waco, Texas |
| Henry W. Cook, M. D. | Minneapolis, Minn. |
| Donald B. Cragin, M. D. | Hartford, Conn. |

## DECEASED MEMBERS

| | |
|---|---|
| Thomas C. Craig, M. D. | New York, N. Y. |
| Hugh W. Crawford, M. D. | Boston, Mass. |
| Hamilton C. Cruikshank, M. D. | Toronto, Canada |
| Edward Curtis, M. D. | New York, N. Y. |
| Clark W. Davis, M. D. | Cincinnati, Ohio |
| William B. Davis, M. D. | Cincinnati, Ohio |
| Charles A. Devendorf, M. D. | Detroit, Mich. |
| Henry K. Dillard, M. D. | Philadelphia, Pa. |
| Frank Donaldson, M. D. | Baltimore, Md. |
| William W. Dow, M. D. | Toronto, Canada |
| Percy G. Drake, M. D. | Hartford, Conn. |
| Edwin W. Dwight, M. D. | Boston, Mass. |
| James B. Eagleson, M. D. | Seattle, Wash. |
| Z. Taylor Emery, M. D. | New York, N. Y. |
| Joseph E. Engelson, M. D. | New York, N. Y. |
| Francis C. Evers, M. D. | New York, N. Y. |
| William G. Exton, M. D. | Newark, N. J. |
| Robert H. Feldt, M. D. | Milwaukee, Wis. |
| W. Ewart Ferguson, M. D. | Toronto, Canada |
| Victor J. Fingar, M. D. | New York, N. Y. |
| John W. Fisher, M. D. | Milwaukee, Wis. |
| Paul FitzGerald, M. D. | Newark, N. J. |
| Thomas A. Foster, M. D. | Portland, Me. |
| Robert A. Fraser, M. D. | New York, N. Y. |
| Samuel W. Gadd, M. D. | Philadelphia, Pa. |
| Homer Gage, M. D. | Worcester, Mass. |
| Thomas H. Gage, M. D. | Worcester, Mass. |
| Donald M. Gedge, M. D. | New York, N. Y. |
| Walter R. Gillette, M. D. | New York, N. Y. |
| Frank S. Grant, M. D. | New York, N. Y. |
| Frederick L. Grasett, M. D. | Toronto, Canada |
| Landon Carter Gray, M. D. | New York, N. Y. |
| Frank L. Grosvenor, M. D. | Hartford, Conn. |
| Frederick W. Hagney, M. D. | Newark, N. J. |

## DECEASED MEMBERS

| | |
|---|---|
| Ignatius Haines, M. D. | Boston, Mass. |
| George C. Hall, M. D. | Richmond, Va. |
| Joseph B. Hall, M. D. | Hartford, Conn. |
| Edward H. Hamill, M. D. | Newark, N. J. |
| William D. Heaton, M. D. | New York, N. Y. |
| William W. Hitchcock, M. D. | Los Angeles, Calif. |
| Angier B. Hobbs, M. D. | New York, N. Y. |
| William W. Hobson, M. D. | Pittsburgh, Pa. |
| Donald C. Hoffman, M. D. | New York, N. Y. |
| Edgar Holden, M. D. | Newark, N. J. |
| John Homans, M. D. | Boston, Mass. |
| John Homans, 2d, M. D. | Boston, Mass. |
| J. Charles Humphreys, M. D. | Philadelphia, Pa. |
| Abel Huntington, M. D. | New York, N. Y. |
| Ross Huston, M. D. | Des Moines, Iowa |
| Henry H. Hutchison, M. D. | Toronto, Canada |
| Lefferts Hutton, M. D. | New York, N. Y. |
| Charles E. Iliff, M. D. | Cincinnati, Ohio |
| Phineas H. Ingalls, M. D. | Hartford, Conn. |
| Charles B. Irwin, M. D. | Chicago, Ill. |
| Arthur Jukes Johnson, M. D. | Toronto, Canada |
| William M. Jones, M. D. | Greensboro, N. C. |
| John M. Keating, M. D. | Philadelphia, Pa. |
| Edward B. Kellogg, M. D. | Boston, Mass. |
| Frank W. Kenney, M. D. | Denver, Colo. |
| Augustus S. Knight, M. D. | New York, N. Y. |
| William W. Knight, M. D. | Hartford, Conn. |
| Edward Lambert, M. D. | New York, N. Y. |
| John B. Lewis, M. D. | Hartford, Conn. |
| Ernest H. Lines, M. D. | New York, N. Y. |
| John M. Little, M. D. | Boston, Mass. |
| G. Carroll Lockard, M. D. | Baltimore, Md. |
| Robert L. Lounsberry, M. D. | Binghamton, N. Y. |
| Carl Lovelace, M. D. | Waco, Texas |

## DECEASED MEMBERS

| | |
|---|---|
| Henry P. Lyster, M. D. | Detroit, Mich. |
| Lewis F. MacKenzie, M. D. | Newark, N. J. |
| Milton T. McCarty, M. D. | Frankfort, Ind. |
| Charles N. McCloud, M. D. | St. Paul, Minn. |
| Carleton B. McCulloch, M. D. | Indianapolis, Ind. |
| Francis A. McGreen, M. D. | New York, N. Y. |
| Lewis McKnight, M. D. | Milwaukee, Wis. |
| Thomas H. McMahon, M. D. | Toronto, Canada |
| Walter T. McNaughton, M. D. | Milwaukee, Wis. |
| William L. Mann, M. D. | Winnipeg, Canada |
| Elias J. Marsh, M. D. | Paterson, N. J. |
| Henry A. Martelle, M. D. | Hartford, Conn. |
| Edward L. Mathias, M. D. | Kansas City, Mo. |
| Allison Maxwell, M. D. | Indianapolis, Ind. |
| Archibald Mercer, M. D. | Newark, N. J. |
| Francis D. Merchant, M. D. | New York, N. Y. |
| William R. Miller, M. D. | Hartford, Conn. |
| William D. Morgan, M. D. | Hartford, Conn. |
| John P. Munn, M. D. | New York, N. Y. |
| William Natress, M. D. | Toronto, Canada |
| Charles T. Necker, M. D. | Waterloo, Canada |
| Edwin M. Northcott, M. D. | Portland, Me. |
| Ralph B. Ober, M. D. | Springfield, Mass. |
| Brace W. Paddock, M. D. | Pittsfield, Mass. |
| Frank K. Paddock, M. D. | Pittsfield, Mass. |
| J. Allen Patton, M. D. | Newark, N. J. |
| William O. Pauli, M. D. | Cincinnati, Ohio |
| William A. Peterson, M. D. | Chicago, Ill. |
| Joseph E. Pollard, M. D. | Newark, N. J. |
| William E. Porter, M. D. | New York, N. Y. |
| Albert T. Post, M. D. | New York, N. Y. |
| James T. Priestly, M. D. | Des Moines, Iowa |
| William W. Quinlan, M. D. | Chicago, Ill. |
| Oliver P. Rex, M. D. | Philadelphia, Pa. |

## DECEASED MEMBERS

| | |
|---|---|
| James A. Roberts, M. D. | Toronto, Canada |
| Thomas H. Rockwell, M. D. | New York, N. Y. |
| Oscar H. Rogers, M. D. | New York, N. Y. |
| Edward K. Root, M. D. | Hartford, Conn. |
| James F. W. Ross, M. D. | Toronto, Canada |
| Charles L. Rudasill, M. D. | Richmond, Va. |
| Gurdon W. Russell, M. D. | Hartford, Conn. |
| Robert Sanderson, M. D. | Boston, Mass. |
| Samuel B. Scholz, M. D. | Philadelphia, Pa. |
| Joseph O. Segura, M. D. | Jackson, Miss. |
| George R. Shepherd, M. D. | Hartford, Conn. |
| Arthur L. Sherrill, M. D. | New York, N. Y. |
| Donald W. Skeel, M. D. | Los Angeles, Calif. |
| Dewitt Smith, M. D. | Dallas, Tex. |
| George S. Stebbins, M. D. | Springfield, Mass. |
| Archibald R. Stone, M. D. | Columbus, Ohio |
| George S. Strathy, M. D. | Toronto, Canada |
| Melancthon Storrs, M. D. | Hartford, Conn. |
| Brandreth Symonds, M. D. | New York, N. Y. |
| H. Cabell Tabb, M. D. | Richmond, Va. |
| Harold F. Taylor, M. D. | Hartford, Conn. |
| James Thorburn, M. D. | Toronto, Canada |
| James D. Thorburn, M. D. | Toronto, Canada |
| William Thorndike, M. D. | Milwaukee, Wis. |
| Paul E. Tiemann, M. D. | New York, N. Y. |
| Harry Toulmin, M. D. | Philadelphia, Pa. |
| Frank L. Truitt, M. D. | Indianapolis, Ind. |
| Henry Tuck, M. D. | New York, N. Y. |
| Henry B. Turner, M. D. | New York, N. Y. |
| John S. Turner, M. D. | Dallas, Tex. |
| Joseph P. Turner, M. D. | Greensboro, N. C. |
| S. Oakley Van der Poel, M. D. | New York, N. Y. |
| Charles A. VanDervoort, M. D. | Philadelphia, Pa. |
| A. L. Vanderwater, M. D. | New York, N. Y. |

## DECEASED MEMBERS

| | |
|---|---|
| Clinton D. W. VanDyck, M. D. | New York, N. Y. |
| George A. VanWagenen, M. D. | Newark, N. J. |
| Aaron C. Ward, M. D. | Newark, N. J. |
| William Perry Watson, M. D. | Newark, N. J. |
| Joseph H. Webb, M. D. | Waterloo, Canada |
| William E. H. Wehner, M. D. | Philadelphia, Pa. |
| Faneuil S. Weisse, M. D. | New York, N. Y. |
| George R. Welch, M. D. | New York, N. Y. |
| Ernest A. Wells, M. D. | Hartford, Conn. |
| Frank Wells, M. D. | Boston, Mass. |
| Franklin C. Wells, M. D. | New York, N. Y. |
| George W. Wells, M. D. | New York, N. Y. |
| Charles D. Wheeler, M. D. | Worcester, Mass. |
| A. H. Whitridge, M. D. | Baltimore, Md. |
| George Wilkins, M. D. | Montreal, Canada |
| Thomas H. Willard, M. D. | New York, N. Y. |
| Charles H. Willits, M. D. | Philadelphia, Pa. |
| Gordon Wilson, M. D. | Baltimore, Md. |
| G. S. Winston, M. D. | New York, N. Y. |
| Harry P. Woley, M. D. | New York, N. Y. |
| Albert Wood, M. D. | Worcester, Mass. |
| Green V. Woolen, M. D. | Indianapolis, Ind. |
| John C. Young, M. D. | Detroit, Mich. |
| Joseph C. Young, M. D. | Newark, N. J. |

## LIST OF MEMBERS OF THE ASSOCIATION OF LIFE INSURANCE MEDICAL DIRECTORS

| | |
|---|---|
| John W. Abbott, M. D. | Paul Revere, Worcester, Mass. |
| Charles B. Ahlefeld, M. D. | Business Men's, Kansas City, Mo. |
| George E. Allen, M. D. | National, Montpelier, Vt. |
| Henry H. Amsden, M. D. | United Life and Accident, Concord, N. H. |
| E. A. Anderson, M. D. | Modern Woodmen, Rock Island, Ill. |
| Karl W. Anderson, M. D. | Northwestern National, Minneapolis, Minn. |
| Perry A. Anderson, M. D. | Rockford Life, Rockford, Ill. |
| Robert L. Anderson, Jr., M. D. | Reliance, Pittsburgh, Pa. |
| Thomas M. Armstrong, M. D. | Philadelphia Life, Philadelphia, Pa. |
| William B. Aten, M. D. | Security Mutual, Binghamton, N. Y. |
| Donald R. Auten, M. D. | New York Life, New York City |
| J. Albert Avrack, M. D. | United States Life, New York City |
| Bernard Baillargeon, M. D. | Alliance Nationale, Montreal, Canada |
| Henry A. Bancel, M. D. | Mutual, New York City |
| G. Holbrook Barber, M. D. | Manhattan, New York City |
| Norman J. Barker, M. D. | Connecticut General, Hartford, Conn. |
| Gordon P. Barnett, M. D. | Kansas City Life, Kansas City, Mo. |
| Charles M. Barrett, M. D. | Western and Southern, Cincinnati, Ohio |

| | |
|---|---|
| Daniel S. Baughman, M. D. | Security Life and Accident, Denver, Colo. |
| Carroll C. Beach, M. D. | State Mutual, Worcester, Mass. |
| J. Randolph Beard, M. D. | Mutual Benefit, Newark, N. J. |
| Edgar W. Beckwith, M. D. | Equitable Life Assurance, New York City |
| James E. Bee, M. D. | Kansas City Life, Kansas City, Mo. |
| Roland A. Behrman, M. D. | John Hancock Mutual, Boston, Mass. |
| J. V. Bell, M. D. | National Fidelity, Kansas City, Mo. |
| Murray F. Bell, M. D. | New York Life, New York City |
| Maurice B. Bender, M. D. | Guardian, New York City |
| Roy W. Benton, M. D. | Northwestern Mutual, Milwaukee, Wis. |
| C. Coleman Berwick, M. D. | Metropolitan, New York City |
| Francis P. Bicknell, M. D. | State Mutual, Worcester, Mass. |
| J. Rozier Biggs, M. D. | Peoples, Washington, D. C. |
| Cecil C. Birchard, M. D. | Sun, Montreal, Canada |
| B. Cosby Bird, M. D. | Preferred, Montgomery, Ala. |
| William R. Bishop, M. D. | Jefferson Standard, Greensboro, N. C. |
| Norman R. Blatherwick, M. D. | Metropolitan, New York City |
| John E. Boland, M. D. | Country, Chicago, Ill. |
| William Bolt, M. D. | New York Life, New York City |
| John M. Bond, M. D. | Northwestern Mutual, Milwaukee, Wis. |
| Earl C. Bonnett, M. D. | Metropolitan, New York City |
| M. Theodore Boss, M. D. | Home Friendly, Baltimore, Md. |
| J. Thornley Bowman, M. D. | London Life, London, Canada |

| | |
|---|---|
| Ernest L. Boylen, M. D. | Standard, Portland, Ore. |
| Kenneth F. Brandon, M. D. | Aetna, Hartford, Conn. |
| Albert W. Bromer, M. D. | Metropolitan, New York City |
| C. Frank Brown, M. D. | Southwestern, Dallas, Texas |
| Frederick R. Brown, M. D. | New England Mutual, Boston, Mass. |
| Howard B. Brown, M. D. | Massachusetts Mutual, Springfield, Mass. |
| Leslie Brown, M. D. | Equitable Life Assurance, New York City |
| William Brueggemann, M. D. | Union Central, Cincinnati, Ohio |
| Ronald F. Buchan, M. D. | Prudential, Newark, N. J. |
| Earl R. Bush, M. D. | Western and Southern, Cincinnati, Ohio |
| Benjamin F. Byrd, M. D. | National Life & Accident, Nashville, Tenn. |
| Joseph T. Cabaniss, M. D. | Travelers, Hartford, Conn. |
| Edward J. Campbell, M. D. | New York Life, New York City |
| Hugh B. Campbell, M. D. | Phoenix Mutual, Hartford, Conn. |
| Paul E. Carlisle, M. D. | Prudential, Los Angeles, Calif. |
| Verne S. Caviness, M. D. | Occidental, Raleigh, N. C. |
| Laurence D. Chapin, M. D. | Massachusetts Mutual, Springfield, Mass. |
| John P. Chapman, M. D. | Girard, Philadelphia, Pa. |
| Paul H. Charlton, M. D. | Midland Mutual, Columbus, Ohio |
| Edmund D. Chesebro, M. D. | Puritan, Providence, R. I. |
| Harry E. Christensen, M. D. | Union Mutual, Portland, Maine |

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|---|---|
| Joseph C. Clifford, M. D. | Aetna, Hartford, Conn. |
| Milton H. Clifford, M. D. | New England Mutual, Boston, Mass. |
| Augustus D. Cloyd, M. D. | Woodmen of the World, Omaha, Neb. |
| Harry A. Cochran, Jr., M. D. | Reliance, Pittsburgh, Pa. |
| Norman B. Cole, M. D. | Baltimore Life, Baltimore, Md. |
| Irwin E. Colgin, M. D. | Texas Life, Waco, Texas |
| Harry L. Colombo, M. D. | National Life, Montpelier, Vt. |
| Frederick R. Congdon, M. D. | Berkshire, Pittsfield, Mass. |
| J. Lindsay Cook, M. D. | Pilot, Greensboro, N. C. |
| Neil L. Criss, M. D. | United Benefit, Omaha, Neb. |
| Howard K. Crutcher, M. D. | United Fidelity, Dallas, Texas |
| Khurshed J. J. Cursetji, M. D. | Oriental Government Security Life, Bombay, India |
| John P. Davis, M. D. | Security Life & Trust, Winston-Salem, N. C. |
| Bryan A. Dawber, M. D. | Penn Mutual, Philadelphia, Pa. |
| John S. Delahaye, M. D. | Empire Life, Kingston, Canada |
| Harold D. Delamere, M. D. | Crown, Toronto, Canada |
| Aniceto Del Rio, M. D. | La Nacional, Mexico City, Mexico |
| J. Emile Desrochers, M. D. | La Sauvegarde, Montreal, Canada |
| Ernest J. Dewees, M. D. | Provident Mutual, Philadelphia, Pa. |
| Earle T. Dewey, M. D. | Metropolitan, New York City |
| Edwin G. Dewis, M. D. | Prudential, Newark, N. J. |
| Edward S. Dillon, M. D. | Penn Mutual, Philadelphia, Pa. |

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|---|---|
| Harold W. Dingman, M. D. | Continental Assurance, Chicago, Ill. |
| Nathaniel P. Doak, M. D. | Great Southern, Houston, Texas |
| Albert H. Domm, M. D. | Prudential, Los Angeles, Calif. |
| James P. Donelan, M. D. | Guarantee Mutual, Omaha, Neb. |
| Gerald D. Dorman, M. D. | New York Life, New York City |
| James T. Downs, Jr., M. D. | Fidelity Union, Dallas, Texas |
| Thomas C. Dunlop, M. D. | Manufacturers, Toronto, Canada |
| Louis B. Dunn, M. D. | Postal, New York City |
| John T. Eads, M. D. | Penn Mutual, Philadelphia, Pa. |
| William W. Eakin, M. D. | Standard, Montreal, Canada |
| Theodore M. Ebers, M. D. | Connecticut Mutual, Hartford, Conn. |
| H. Glenn Ebersole, M. D. | Illinois Bankers, Monmouth, Ill. |
| Laurence B. Ellis, M. D. | Boston Mutual, Boston, Mass. |
| Jack A. End, M. D. | Northwestern Mutual, Milwaukee, Wis. |
| John A. Evans, M. D. | Metropolitan, New York City |
| John L. Evans, M. D. | Farmers & Bankers, Wichita, Kan. |
| Albert H. Faber, M. D. | New York Life, New York City |
| J. Gilbert Falconer, M. D. | North American, Toronto, Canada |
| Raymond K. Farnham, M. D. | Metropolitan, New York City |
| Haynes H. Fellows, M. D. | Metropolitan, New York City |
| William S. Fewell, M. D. | Liberty, Greenville, S. C. |

| | |
|---|---|
| Ralph M. Filson, M. D. | Travelers, Hartford, Conn. |
| Rexford W. Finegan, M. D. | Metropolitan, New York City |
| Frederick Fink, M. D. | Franklin, Springfield, Ill. |
| Harry E. Flansburg, M. D. | Bankers, Lincoln, Neb. |
| Philip M. L. Forsberg, M. D. | United Life and Accident, Concord, N. H. |
| Garth E. Fort, M. D. | National Life & Accident, Nashville, Tenn. |
| John M. Foster, M. D. | Capitol, Denver, Colo. |
| Edward M. Freeland, M. D. | New York Life, New York City |
| Dale G. Friend, M. D. | John Hancock Mutual, Boston, Mass. |
| Clarence E. Fronk, M. D. | Hawaiian Life, Honolulu, T. H. |
| Harold M. Frost, M. D. | New England Mutual, Boston, Mass. |
| F. Irving Ganot, M. D. | Prudential, Newark, N. J. |
| I. Kenneth Gardner, M. D. | Reliance, Pittsburgh, Pa. |
| David S. Garner, M. D. | Shenandoah, Roanoke, Va. |
| J. H. Geddes, M. D. | Northern, London, Canada |
| John T. Geiger, M. D. | Metropolitan, New York City |
| William M. Genthner, M. D. | Continental American, Wilmington, Del. |
| Edson E. Getman, M. D. | New York Life, New York City |
| John M. Gilchrist, M. D. | Monarch, Springfield, Mass. |
| Ralph T. Gilchrist, M. D. | Northwestern Mutual, Milwaukee, Wis. |
| Edgar G. Givhan, Jr., M. D. | Protective, Birmingham, Ala. |
| Robert A. Goodell, M. D. | Phoenix Mutual, Hartford, Conn. |

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| George Goodkin, M. D. | Equitable Life Assurance, New York City |
| Harry W. Goos, M. D. | Home, Philadelphia, Pa. |
| J. Keith Gordon, M. D. | Sun, Montreal, Canada |
| Douglas M. Gover, M. D. | Franklin, Springfield, Ill. |
| Angus S. Graham, M. D. | London Life, London, Canada |
| George M. Graham, M. D. | Lincoln National, Fort Wayne, Ind. |
| Ghent Graves, M. D. | American General, Houston, Texas |
| Marvin L. Graves, M. D. | American General, Houston, Texas |
| Robert J. Graves, M. D. | United Life and Accident, Concord, N. H. |
| Harris M. Gray, M. D. | Manufacturers, Toronto, Canada |
| Floyd M. Green, M. D. | Columbus Mutual, Columbus, Ohio. |
| George E. Greenway, M. D. | Western Life Assurance, Hamilton, Canada |
| C. J. M. Grisdale, M. D. | Connecticut General, Hartford, Conn. |
| Frederick O. Gronvold, M. D. | Pioneer Mutual, Fargo, N. D. |
| Richard S. Gubner, M. D. | Equitable Life Assurance, New York City |
| James R. Gudger, M. D. | Mutual, New York City |
| David Halbersleben, M. D. | John Hancock Mutual, Boston, Mass. |
| Llewellyn Hall, M. D. | Phoenix Mutual, Hartford, Conn. |
| F. Tulley Hallam, M. D. | State, Indianapolis, Ind. |
| John H. Halliday, M. D. | Australian Mutual, Sydney Australia |
| Gerald W. Halpenny, M. D. | Royal, Montreal, Canada |
| Vincent G. Hammond, M. D. | Security Mutual, Binghamton, N. Y. |

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| Ottis E. Hanes, M. D. | Life Ins. Co. of Ga., Atlanta, Ga. |
| Charles P. Hardwicke, M. D. | Western Reserve, Austin, Texas |
| Frank Harnden, M. D. | Berkshire, Pittsfield, Mass. |
| Garland M. Harwood, M. D. | Life Insurance Co. of Virginia, Richmond, Va. |
| Louis E. Hathaway, Jr., M. D. | Monarch, Springfield, Mass. |
| Howard L. Hauge, M. D. | New York Life, New York City |
| Walter C. Hausheer, M. D. | Prudential, Newark, N. J. |
| Harry M. Hawkins, M. D. | Old Line, Milwaukee, Wis. |
| Thomas L. Hawkins, M. D. | Western, Helena, Mont. |
| Joseph K. P. Hawks, M. D. | State Farm, Bloomington, Ill. |
| J. Harry Hayes, M. D. | Union, Little Rock, Ark. |
| Ernest M. Henderson, M. D. | Confederation, Toronto, Canada |
| Olin C. Hendrix, M. D. | New England Mutual, Boston, Mass. |
| Charles R. Henry, M. D. | Provident Life and Accident Chattanooga, Tenn. |
| Andrew C. Henske, M. D. | Mutual Savings, St. Louis, Mo. |
| Ivan C. Heron, M. D. | West Coast, San Francisco, Calif. |
| Eugene V. Higgins, M. D. | Manhattan, New York City |
| William L. Hilliard, M. D. | Equitable, Waterloo, Canada |
| Ernest C. Hillman, Jr., M. D. | Mutual Benefit, Newark, N. J. |
| Daniel W. Hoare, M. D. | Penn Mutual, Philadelphia, Pa. |
| Ira E. Hoffman, M. D. | Washington National, Evanston, Ill. |
| Joseph C. Horan, M. D. | Metropolitan, New York City |
| Edward G. Howe, M. D. | Prudential, Newark, N. J. |

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| Thomas B. Hoxie, M. D. | New York Life, New York City |
| Henry W. Hudson, M. D. | Loyal Protective, Boston, Mass. |
| John L. Humphreys, M. D. | Reliance, Pittsburgh, Pa. |
| James H. Humphries, M. D. | Home, New York City |
| J. Edward Hunsinger, M. D. | Republic Nat'l, Dallas, Texas |
| Benjamin L. Huntington, M. D. | John Hancock Mutual, Boston, Mass. |
| Samuel W. Hurdle, M. D. | Security Life & Trust, Winston-Salem, N. C. |
| John J. Hutchinson, M. D. | New York Life, New York City |
| J. Raymond B. Hutchinson, M. D. | Acacia Mutual, Washington, D. C. |
| William G. Hyde, M. D. | Northwestern Mutual, Milwaukee, Wis. |
| Albert S. Irving, M. D. | Commonwealth, Louisville, Ky. |
| J. Grant Irving, M. D. | Aetna, Hartford, Conn. |
| Samuel Jagoda, M. D. | State Reserve, Fort Worth, Texas |
| Albert O. Jimenis, M. D. | Metropolitan, New York City |
| Albert E. Johann, M. D. | Bankers, Des Moines, Iowa |
| Hubert R. John, M. D. | Maccabees, Detroit, Mich. |
| Joseph W. Johnson, Jr., M. D. | Interstate Life and Accident, Chattanooga, Tenn. |
| Victor L. Karren, M. D. | Home, New York City |
| Edward A. Keenleyside, M. D. | Connecticut General, Hartford, Conn. |
| Charles H. Kelley, M. D. | Columbian National, Boston, Mass. |

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| Newell R. Kelley, M. D. | Phoenix Mutual, Hartford, Conn. |
| Herbert B. Kennedy, M. D. | Woodmen of the World, Omaha, Neb. |
| Harry B. Kidd, M. D. | Metropolitan, New York City |
| Charles E. Kiessling, M. D. | Prudential, Newark, N. J. |
| Donald G. Kilgore, M. D. | Republic National, Dallas, Texas |
| Ray E. King, M. D. | Bankers, Des Moines, Iowa |
| Henry B. Kirkland, M. D. | Prudential, Newark, N. J. |
| Edward Kuck, M. D. | Union Central, Cincinnati, Ohio |
| Earl J. Kuenster, M. D. | Paul Revere, Worcester, Mass. |
| Paul Kurzweg, Jr., M. D. | All American Assurance, Lafayette, La. |
| Walter C. Lamb, M. D. | Equitable Life Assurance, New York City |
| Phillips Lambkin, M. D. | Guardian, New York City |
| Paul H. Langner, Jr., M. D. | Provident Mutual, Philadelphia, Pa. |
| Louis G. LaPointe, M. D. | Equitable Life Assurance, New York City |
| H. Franklyn Laramore, M. D. | Connecticut Mutual, Hartford, Conn. |
| Rodney C. Larcom, Jr., M. D. | John Hancock Mutual, Boston, Mass. |
| Albert L. Larson, M. D. | Travelers, Hartford, Conn. |
| Ivan C. Lawler, M. D. | New York Life, New York City |
| Linford H. Lee, M. D. | Pacific Mutual, Los Angeles, Calif. |
| Edward P. Leeper, M. D. | Praetorians, Dallas, Texas |
| Harold R. Leffingwell, M. D. | Paul Revere, Worcester, Mass. |
| William R. Leute, Jr., M. D. | Penn Mutual, Philadelphia, Pa. |

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| T. Herbert Lewis, M. D. | Western States, Fargo, N. D. |
| George G. Lindsay, M. D. | Scranton Life, Scranton, Pa. |
| Everett H. Lindstrom, M. D. | Western, Helena, Mont. |
| James A. Livingston, M. D. | Liberty National, Birmingham, Ala. |
| John M. Livingston, M. D. | Mutual, Waterloo, Canada |
| Gladstone W. Lougheed, M. D. | Confederation, Toronto, Canada |
| Cabot Lull, M. D. | American, Birmingham, Ala. |
| Gerald J. Lunz, M. D. | Knights of Columbus, New Haven, Conn. |
| H. Clive McAlister, M. D. | Lincoln National, Ft. Wayne, Ind. |
| Frank M. McChesney, M. D. | Equitable, Washington, D. C. |
| William J. McConnell, M. D. | Metropolitan, New York City |
| George McCreight, M. D. | Bankers, Des Moines, Iowa |
| John G. MacDougall, M. D. | Maritime, Halifax, Canada |
| Arthur J. McGanity, M. D. | Dominion, Waterloo, Canada |
| Frank J. McGurl, M. D. | Prudential, Newark, N. J. |
| William G. McLaughry, M. D. | Protected Home Circle, Sharon, Pa. |
| George McLean, M. D. | Sun, Baltimore, Md. |
| Lawrence L. McLellan, M. D. | Provident Mutual, Philadelphia, Pa. |
| Ralph E. McLochlin, M. D. | National Old Line, Little Rock, Ark. |
| Asher R. McMahan, M. D. | Columbian Mutual, Memphis, Tenn. |
| William J. McNamara, M. D. | Equitable Life Assurance, New York City |
| Charles Maertz, M. D. | Union Central, Cincinnati, Ohio |

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| Charles D. Magee, M. D. | Missouri Insurance Company, St. Louis, Mo. |
| S. J. Newton Magwood, M. D. | Continental, Toronto, Canada |
| Robert W. Mann, M. D. | Imperial, Toronto, Canada |
| Francis A. L. Mathewson, M. D. | Monarch, Winnipeg, Canada |
| Loren K. Meredith, M. D. | National, Des Moines, Iowa |
| Ignacio Mesa, M. D. | "La Latino-Americana", Mexico City, Mexico |
| Ernest B. Milan, M. D. | Peninsular, Jacksonville, Fla. |
| Lloyd C. Miller, M. D. | National Life & Accident, Nashville, Tenn. |
| Edward S. Mills, M. D. | Prudential Assurance, Montreal, Canada |
| Eugene Montgomery, M. D. | North American, Toronto, Canada |
| James T. Montgomery, M. D. | North American Reassurance, New York City |
| Richard C. Montgomery, M. D. | Manufacturers, Toronto, Canada |
| John F. Moore, Jr., M. D. | Mutual, New York City |
| J. R. E. Morden, M. D. | Massachusetts Mutual, Springfield, Mass. |
| Reuben A. Moser, M. D. | American Reserve, Omaha Neb. |
| Bernard Mount, M. D. | All States, Montgomery, Alabama |
| Elmer B. Mountain, M. D. | American Mutual, Des Moines, Iowa |
| Clifford V. Mulligan, M. D. | T. Eaton, Toronto, Canada |
| Frederick D. Munroe, M. D. | Fidelity, Regina, Canada |
| Sidney A. Narins, M. D. | Mutual, New York City |
| Clive P. Neilson, M. D. | Sovereign Life, Winnipeg, Canada |

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| Richard A. Nelson, M. D. | Prudential, Newark, N. J. |
| Charles F. Nichols, M. D. | Penn Mutual, Philadelphia, Pa. |
| John B. Nichols, M. D. | Acacia Mutual, Washington, D. C. |
| Richard E. Nicholson, M. D. | Connecticut Mutual, Hartford, Conn. |
| E. Clark Noble, M. D. | National, Toronto, Canada |
| Andrew J. Oberlander, M. D. | National, Montpelier, Vt. |
| William L. O'Connell, M. D. | Union Labor, New York City |
| Martin I. Olsen, M. D. | Central, Des Moines, Iowa |
| Baldur H. Olson, M. D. | Great-West, Winnipeg, Canada |
| William F. H. O'Neill, M. D. | Great-West, Winnipeg, Canada |
| Wilbert C. Page, M. D. | Prudential, Newark, N. J. |
| Charles B. Parker, M. D. | Independent Order of Foresters, Toronto, Canada |
| Arthur E. Parks, M. D. | Canada Life, Toronto, Canada |
| John M. Peck, M. D. | Fidelity Mutual, Philadelphia, Pa. |
| D. Sergeant Pepper, M. D. | Provident Mutual, Philadephia, Pa. |
| Gilberto S. Pesquera, M. D. | Metropolitan, New York City |
| Charles A. Peters, M. D. | Prudential Assurance, Montreal, Canada |
| Cullen Pitt, M. D. | Atlantic, Richmond, Va. |
| John J. Post, M. D. | Life and Casualty, Nashville, Tenn. |
| Roscoe W. Pratt, M. D. | New York Life, New York City |
| William O. Purdy, M. D. | Equitable, Des Moines, Iowa |
| Louis A. Pyle, M. D. | Colonial, East Orange, N. J. |

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| Edwin J. Quinn, M. D. | Mutual, New York City |
| O. Samuel Randall, M. D. | Midland National, Watertown, S. D. |
| Paul M. Rattan, M. D. | Great National, Dallas, Texas |
| James H. Ready, M. D. | General American, St. Louis, Mo. |
| Rezin Reagan, M. D. | Policyholder's National, Sioux Falls, S. D. |
| Clifton L. Reeder, M. D. | Continental Assurance, Chicago, Ill. |
| H. Maynard Rees, M. D. | John Hancock Mutual, Boston, Mass. |
| Paul V. Reinartz, M. D. | Prudential, Newark, N. J. |
| Walter A. Reiter, M. D. | Mutual Benefit, Newark, N. J. |
| Whitman M. Reynolds, M. D. | Equitable Life Assurance, New York City |
| Wallace R. Richardson, M. D. | National Equity, Little Rock, Ark. |
| H. Guy Riche, M. D. | Guaranty Income, Baton Rouge, La. |
| Donald F. Rikkers, M. D. | Northwestern Mutual, Milwaukee, Wis. |
| George P. Robb, M. D. | Metropolitan, New York City |
| David C. Roberts, M. D. | Guardian, New York City |
| Albert J. Robinson, M. D. | Connecticut General, Hartford, Conn. |
| Claude A. Robison, M. D. | Peoples, Frankfort, Ind. |
| Henry B. Rollins, M. D. | Connecticut Mutual, Hartford, Conn. |
| Fred W. Rolph, M. D. | Confederation, Toronto, Canada |
| Gordon Ross, M. D. | Massachusetts Mutual, Springfield, Mass. |
| John G. Ross, M. D. | Mutual, Waterloo, Canada |
| Thomas F. Ross, M. D. | Ohio State, Columbus, Ohio |
| Edward W. Rowe, M. D. | Midwest, Lincoln, Neb. |

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| James M. H. Rowland, M. D. | Baltimore Life, Baltimore, Md. |
| Robert L. Rowley, M. D. | Phoenix Mutual, Hartford, Conn. |
| William W. Rucks, M. D. | Home State, Oklahoma City, Okla. |
| Dan Y. Sage, M. D. | Southern, Atlanta, Ga. |
| Joe H. Sanderlin, M. D. | Pyramid, Little Rock, Ark. |
| Raymond C. Scannell, M. D. | Security Life and Accident, Denver, Colo. |
| Kenneth F. Schaefer, M. D. | Prudential, Newark, N. J. |
| Berthold T. D. Schwarz, M. D. | Bankers National, Montclair, N. J. |
| William H. Scoins, M. D. | Lincoln National, Ft. Wayne, Ind. |
| Robert J. Scott, M. D. | Michigan Life, Detroit, Mich. |
| Albert Seaton, M. D. | American United, Indianapolis, Ind. |
| Ralph C. Secor, M. D. | Connecticut Mutual, Hartford, Conn. |
| Alfred F. Seibert, M. D. | Travelers, Hartford, Conn. |
| David L. Selby, M. D. | Imperial, Toronto, Canada |
| Thomas S. Sexton, M. D. | Massachusetts Mutual, Springfield, Mass. |
| Hall Shannon, M. D. | Southland, Dallas, Texas |
| Elroy F. Sheldon, M. D. | Occidental, Los Angeles, Calif. |
| Joyce T. Sheridan, M. D. | Fidelity Mutual, Philadephia, Pa. |
| Daniel M. Shewbrooks, M. D. | Penn Mutual, Philadelphia, Pa. |
| Hubert H. Shook, M. D. | Ohio National, Cincinnati, Ohio |
| Ralph R. Simmons, M. D. | Equitable, Des Moines, Iowa |
| F. Hartley Smith, M. D. | Great-West, Winnipeg, Canada |
| Stewart A. Smith, M. D. | Australian Mutual, Sydney, Australia |

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| Wilbur A. Smith, M. D. | Equitable Life Assurance, New York City |
| Isaac Sossnitz, M. D. | Eastern, New York City |
| Marion Souchon, M. D. | Pan-American, New Orleans, La. |
| Charles G. Spivey, M. D. | Carolina Life, Columbia, S. C. |
| Frank L. Springer, M. D. | Columbian National, Boston, Mass. |
| H. Frank Starr, M. D. | Jefferson Standard, Greensboro, N. C. |
| F. R. Stearns, M. D. | Security Benefit Association, Topeka, Kan. |
| George G. Stebbins, M. D. | Wisconsin Life, Madison, Wis. |
| John B. Steele, M. D. | Volunteer State, Chattanooga, Tenn. |
| David F. R. Steuart, M. D. | Mutual Benefit, Newark, N. J. |
| Edgar M. Stevenson, M. D. | State Farm, Bloomington, Ill. |
| Hector M. Stevenson, M. D. | Aetna, Hartford, Conn. |
| Lester Q. Stewart, M. D. | Aetna, Hartford, Conn. |
| I. Read Stidger, M. D. | Prudential, Newark, N. J. |
| Frank M. Stites, M. D. | Kentucky Home Mutual, Louisville, Ky. |
| Samuel J. Streight, M. D. | Canada Life, Toronto, Canada |
| Nicholas A. Sullo, M. D. | Equitable Life Assurance, New York City. |
| Bion C. Syverson, M. D. | Equitable Life Assurance, New York City |
| Louis J. Tedesco, M. D. | New York Life, New York City |
| Gamber F. Tegtmeyer, M. D. | Northwestern Mutual, Milwaukee, Wis. |
| Edward R. Thompson, M. D. | Texas Prudential, Galveston, Texas |
| Hugh G. Thompson, M. D. | George Washington, Charleston, W. Va. |

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| K. Jefferson Thomson, M. D. | Metropolitan, New York City |
| William B. Thornton, M. D. | Norwich Union, Toronto, Canada |
| Albert R. Tormey, M. D. | National Guardian, Madison, Wis. |
| Grafton D. Townshend, M. D. | Standard Life Association, Lawrence, Kansas |
| Joseph Travenick, Jr., M. D. | Occidental, Los Angeles, Calif. |
| Wallace Troup, M. D. | Metropolitan, New York City |
| Francis D. Truax, M. D. | Crown, Toronto, Canada |
| Maurice Turcotte, M. D. | Industrial, Quebec, Canada |
| Harry E. Ungerleider, M. D. | Equitable Life Assurance, New York City |
| Bruce W. Vale, M. D. | Excelsior, Toronto, Canada |
| Euen Van Kleeck, M. D. | Travelers, Hartford, Conn. |
| Alexander E. Venables, M. D. | Minnesota Mutual, St. Paul, Minn. |
| Frederick H. Vinup, M. D. | Monumental, Baltimore, Md. |
| Reynold C. Voss, M. D. | Pan-American, New Orleans, La. |
| Murray Wagman, M. D. | Mutual Benefit, Newark, N. J. |
| Frederick A. Waldron, M. D. | Mutual, New York City |
| George H. Walker, M. D. | Lincoln Liberty, Lincoln, Neb. |
| Dick P. Wall, M. D. | American National, Galveston, Texas |
| Gordon K. Wallace, M. D. | Great American Reserve, Dallas, Tex. |
| Kenneth E. Ward, M. D. | Connecticut General, Hartford, Conn. |

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| R. Vance Ward, M. D. | Montreal Life, Montreal, Canada |
| Frank A. Warner, M. D. | John Hancock Mutual, Boston, Mass. |
| Robert L. Weaver, M. D. | Penn Mutual, Philadelphia, Pa. |
| Jefferson Weed, M. D. | Mutual Benefit, Newark, N. J. |
| John H. Weidner, M. D. | Prudential, Newark, N. J. |
| David E. W. Wenstrand, M. D. | Northwestern Mutual, Milwaukee, Wis. |
| Stephen S. Werth, M. D. | Globe, Chicago, Ill. |
| Howard E. Wiley, M. D. | Southwestern, Dallas, Texas |
| John A. Wilhelm, M. D. | Gulf, Jacksonville, Fla. |
| Alfred A. Willander, M. D. | Mutual Trust, Chicago, Ill. |
| Earl B. Williams, M. D. | Wisconsin National, Oshkosh, Wis. |
| Ennion S. Williams, M. D. | Life Insurance Co. of Virginia, Richmond, Va. |
| Richard L. Willis, M. D. | Mutual, New York City |
| Archibald C. Wilson, M. D. | Connecticut General, Hartford, Conn. |
| C. L. Wilson, M. D. | Empire State Mutual, Jamestown, N. Y. |
| Edmund W. Wilson, M. D. | Metropolitan, New York City |
| Don J. Wolfram, M. D. | Jefferson National, Indianapolis, Ind. |
| George E. Woodford, M. D. | Home, New York City |
| Lauritz S. Ylvisaker, M. D. | Fidelity Mutual, Philadelphia, Pa. |
| Donald E. Yochem, M. D. | Farm Bureau, Columbus, Ohio |
| Arthur W. Young, M. D. | Sun, Montreal, Canada |
| George G. Young, M. D. | Central, Des Moines, Iowa |
| Victor H. Young, M. D. | Travelers, Hartford, Conn. |
| Russell W. Zinkann, M. D. | Mutual, Waterloo, Canada |

## HONORARY MEMBERS

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| Francis R. Dieuaide, M. D. | New York City |
| Arthur Hunter | New York City |
| Edward E. Rhodes | Newark, N. J. |

## EMERITUS MEMBERS

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| Edwin H. Allen, M. D. | Boston, Mass. |
| Thomas D. Archibald, M. D. | Toronto, Canada |
| William B. Bartlett, M. D. | Boston, Mass. |
| Chester T. Brown, M. D. | Newark, N. J. |
| Robert M. Daley, M. D. | New York City |
| O. M. Eakins, M. D. | Pittsburgh, Pa. |
| George A. Harlow, M. D. | Milwaukee, Wis. |
| Byam Hollings, M. D. | Boston, Mass. |
| Walter A. Jaquith, M. D. | Columbus, Ohio |
| George E. Kanouse, M. D. | Newark, N. J. |
| Francis H. McCrudden, M. D. | Boston, Mass. |
| William Muhlberg, M. D. | Cincinnati, Ohio |
| Herbert Old, M. D. | Philadelphia, Pa. |
| George P. Paul, M. D. | Hartford, Conn. |
| Charles B. Piper, M. D. | Hartford, Conn. |
| H. Crawford Scadding, M. D. | Toronto, Canada |
| Henry H. Schroeder, M. D. | New York City |
| Walter E. Thornton, M. D. | Fort Wayne, Ind. |
| William R. Ward, M. D. | Newark, N. J. |
| Fred L. Wells, M. D. | Des Moines, Iowa |
| Chester F. S. Whitney, M. D. | New York City |
| McLeod C. Wilson, M. D. | Hartford, Conn. |

## COMPANIES AND THEIR REPRESENTATIVES

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| Acacia Mutual Life Insurance Co., Washington, D. C. | J. R. B. Hutchinson, M. D.<br>J. B. Nichols, M. D. |
| Aetna Life Insurance Co., Hartford, Conn. | K. F. Brandon, M. D.<br>J. C. Clifford, M. D.<br>J. G. Irving, M. D.<br>H. M. Stevenson, M. D.<br>L. Q. Stewart, M. D. |
| Alliance Nationale, Montreal, Canada | Bernard Baillargeon, M. D. |
| All American Assurance Co., Lafayette, La. | Paul Kurzweg, Jr., M. D. |
| All States Life Insurance Co., Montgomery, Ala. | Bernard Mount, M. D. |
| American General Life Insurance Co., Houston, Texas | Ghent Graves, M. D.<br>M. L. Graves, M. D. |
| American Life Insurance Co., Birmingham, Ala. | Cabot Lull, M. D. |
| American Mutual Life Insurance Co., Des Moines, Iowa. | E. B. Mountain, M. D. |
| American National Insurance Co., Galveston, Texas. | D. P. Wall, M. D. |
| American Reserve Life Insurance Co., Omaha, Neb. | R. A. Moser, M. D. |
| American United Life Insurance Co., Indianapolis, Ind. | Albert Seaton, M. D. |

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| Atlantic Life Insurance Co., Richmond, Va. | Cullen Pitt, M. D. |
| Australian Mutual Provident Society, Sydney, Australia. | J. H. Halliday, M. D.<br>S. A. Smith, M. D. |
| Baltimore Life Insurance Co., Baltimore, Md. | N. B. Cole, M. D.<br>J. M. H. Rowland, M. D. |
| Bankers Life Company, Des Moines, Iowa. | A. E. Johann, M. D.<br>George McCreight, M. D.<br>R. E. King, M. D. |
| Bankers Life Insurance Co. of Nebraska, Lincoln, Neb. | H. E. Flansburg, M. D. |
| Bankers National Life Ins. Co., Montclair, N. J. | B. T. D. Schwarz, M. D. |
| Berkshire Life Insurance Co., Pittsfield, Mass. | F. R. Congdon, M. D.<br>Frank Harnden, M. D. |
| Boston Mutual Life Insurance Co., Boston, Mass. | L. B. Ellis, M. D. |
| Business Men's Assurance Co. of America, Kansas City, Mo. | C. B. Ahlefeld, M. D. |
| Canada Life Assurance Co., Toronto, Canada. | A. E. Parks, M. D.<br>S. J. Streight, M. D. |
| Capitol Life Insurance Co. of Colorado, Denver, Colo. | J. M. Foster, M. D. |
| Carolina Life Insurance Co., Columbia, S. C. | C. G. Spivey, M. D. |
| Central Life Assurance Society, Des Moines, Iowa. | M. I. Olsen, M. D.<br>G. G. Young, M. D. |
| Colonial Life Insurance Co., East Orange, N. J. | L. A. Pyle, M. D. |

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| Columbian Mutual Life Insurance Co., Memphis, Tenn. | A. R. McMahan, M. D. |
| Columbian National Life Ins. Co., Boston, Mass. | C. H. Kelley, M. D.<br>F. L. Springer, M. D. |
| Columbus Mutual Life Ins. Co., Columbus, Ohio. | F. M. Green, M. D. |
| Commonwealth Life Insurance Co., Louisville, Ky. | A. S. Irving, M. D. |
| Confederation Life Association, Toronto, Canada. | E. M. Henderson, M. D.<br>G. W. Lougheed, M. D.<br>F. W. Rolph, M. D. |
| Connecticut General Life Ins. Co., Hartford, Conn. | N. J. Barker, M. D.<br>C. J. M. Grisdale, M. D.<br>E. A. Keenleyside, M. D.<br>A. J. Robinson, M. D.<br>K. E. Ward, M. D.<br>A. C. Wilson, M. D. |
| Connecticut Mutual Life Ins. Co., Hartford, Conn. | T. M. Ebers, M. D.<br>H. F. Laramore, M. D.<br>R. E. Nicholson, M. D.<br>H. B. Rollins, M. D.<br>R. C. Secor, M. D. |
| Continental Amer. Life Ins. Co., Wilmington, Del. | W. M. Genthner, M. D. |
| Continental Assurance Co., Chicago, Ill. | H. W. Dingman, M. D.<br>C. L. Reeder, M. D. |
| Continental Life Insurance Co., Toronto, Canada. | S. J. N. Magwood, M. D. |
| Country Life Insurance Co., Chicago, Ill. | J. E. Boland, M. D. |
| Crown Life Insurance Co., Toronto, Canada. | H. D. Delamere, M. D.<br>F. D. Truax, M. D. |
| Dominion Life Assurance Co., Waterloo, Canada | A. J. McGanity, M. D. |

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| Eastern Life Insurance Co., New York City | Isaac Sossnitz, M. D. |
| Empire Life Insurance Co., Kingston, Canada | J. S. Delahaye, M. D. |
| Empire State Mutual Life Insurance Co., Jamestown, N. Y. | C. L. Wilson, M. D. |
| Equitable Life Assurance Society, New York City | E. W. Beckwith, M. D.<br>Leslie Brown, M. D.<br>George Goodkin, M. D.<br>R. S. Gubner, M. D.<br>W. C. Lamb, M. D.<br>L. G. LaPointe, M. D.<br>W. J. McNamara, M. D.<br>W. M. Reynolds, M. D.<br>W. A. Smith, M. D.<br>N. A. Sullo, M. D.<br>B. C. Syverson, M. D.<br>H. E. Ungerleider, M. D. |
| Equitable Life Insurance Co., Washington, D. C. | F. M. McChesney, M. D. |
| Equitable Life Ins. Co. of Canada, Waterloo, Canada | W. L. Hilliard, M. D. |
| Equitable Life Insurance Co. of Iowa, Des Moines, Iowa. | W. O. Purdy, M. D.<br>R. R. Simmons, M. D. |
| Excelsior Life Insurance Co., Toronto, Canada. | B. W. Vale, M. D. |
| Farm Bureau Life Ins. Co., Columbus, Ohio. | D. E. Yochem, M. D. |
| Farmers & Bankers Life Insurance Co., Wichita, Kan. | J. L. Evans, M. D. |
| Fidelity Life Assurance Co., Regina, Canada | F. D. Munroe, M. D. |

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| Fidelity Mutual Life Ins. Co., Philadelphia, Pa. | J. M. Peck, M. D.<br>J. T. Sheridan, M. D.<br>L. S. Ylvisaker, M. D. |
| Fidelity Union Life Insurance Co., Dallas, Texas | J. T. Downs, Jr., M. D. |
| Franklin Life Ins. Co., Springfield, Ill. | Frederick Fink, M. D.<br>D. M. Gover, M. D. |
| General American Life Ins. Co., St. Louis, Mo. | J. H. Ready, M. D. |
| George Washington Life Insurance Co., Charleston. W. Va. | H. G. Thompson, M. D. |
| Girard Life Insurance Co., Philadelphia, Pa. | J. P. Chapman, M. D. |
| Globe Life Insurance Co., Chicago, Ill. | S. S. Werth, M. D. |
| Great American Reserve Insurance Co., Dallas, Tex. | G. K. Wallace, M. D. |
| Great National Life Insurance Co., Dallas, Texas | P. M. Rattan, M. D. |
| Great Southern Life Ins. Co., Houston, Texas | N. P. Doak, M. D. |
| Great-West Life Assur. Co., Winnipeg, Canada. | B. H. Olson, M. D.<br>W. F. H. O'Neill, M. D.<br>F. H. Smith, M. D. |
| Guarantee Mutual Life Insurance Co., Omaha, Neb. | J. P. Donelan, M. D. |
| Guaranty Income Life Insurance Co., Baton Rouge, La. | H. G. Riche, M. D. |
| Guardian Life Insurance Co. of America, New York City | M. B. Bender, M. D.<br>Phillips Lambkin, M. D.<br>D. C. Roberts, M. D. |

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| Home State Life Insurance Co., Oklahoma City, Okla. | W. W. Rucks, M. D. |
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| Loyal Protective Life Insurance Co., Boston, Mass. | H. W. Hudson, M. D. |

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| National Guardian Life Insurance Co., Madison, Wis. | A. R. Tormey, M. D. |
| National Life & Accident Ins. Co., Nashville, Tenn. | B. F. Byrd, M. D.<br>G. E. Fort, M. D.<br>L. C. Miller, M. D. |
| National Life Assurance Co. of Canada, Toronto, Canada | E. C. Noble, M. D. |
| National Life Co., Des Moines, Iowa | L. K. Meredith, M. D. |
| National Life Insurance Co., Montpelier, Vt. | G. E. Allen, M. D.<br>H. L. Colombo, M. D.<br>A. J. Oberlander, M. D. |
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| Norwich Union Life Insurance Society, Toronto, Canada | W. B. Thornton, M. D. |
| Occidental Life Insurance Co., Raleigh, N. C. | V. S. Caviness, M. D. |

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| Ohio State Life Insurance Co., Columbus, Ohio | T. F. Ross, M. D. |
| Old Line Life Insurance Co. of America, Milwaukee, Wis. | H. M. Hawkins, M. D. |
| Oriental Government Security Life Assurance Co., Ltd., Bombay, India. | K. J. J. Cursetji, M. D. |
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| Peninsular Life Insurance Co., Jacksonville, Fla. | E. B. Milam, M. D. |
| Penn Mutual Life Ins. Co., Philadelphia, Pa. | B. A. Dawber, M. D.<br>E. S. Dillon, M. D.<br>J. T. Eads, M. D.<br>D. W. Hoare, M. D.<br>W. R. Leute, Jr., M. D.<br>C. F. Nichols, M. D.<br>D. M. Shewbrooks, M. D.<br>R. L. Weaver, M. D. |
| Peoples Life Ins. Co., Frankfort, Ind. | C. A. Robison, M. D. |
| Peoples Life Insurance Co., Washington, D. C. | J. R. Biggs, M. D. |

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| Philadelphia Life Ins. Co., Philadelphia, Pa. | T. M. Armstrong, M. D. |
| Phoenix Mutual Life Ins. Co., Hartford, Conn. | H. B. Campbell, M. D.<br>R. A. Goodell, M. D.<br>Llewellyn Hall, M. D.<br>N. R. Kelley, M. D.<br>R. L. Rowley, M. D. |
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| Royal Insurance Co., Ltd., Montreal, Canada | G. W. Halpenny, M. D. |
| Scranton Life Insurance Co., Scranton. Pa. | G. G. Lindsay, M. D. |
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| Security Life and Accident Co., Denver, Colo. | D. S. Baughman, M. D.<br>R. C. Scannell, M. D. |

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| Southwestern Life Ins. Co., Dallas, Texas | C. F. Brown, M. D.<br>H. E. Wiley, M. D. |
| Sovereign Life Assurance Co., Winnipeg, Canada | C. P. Neilson, M. D. |
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| Sun Life Assurance Company of Canada, Montreal, Canada | C. C. Birchard, M. D.<br>J. K. Gordon, M. D.<br>A. W. Young, M. D. |

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| United Fidelity Life Insurance Co., Dallas, Texas | H. K. Crutcher, M. D. |
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| Western Life Assurance Company, Hamilton, Canada | G. E. Greenway, M. D. |
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| Western States Life Insurance Company, Fargo, N. D. | T. H. Lewis, M. D. |
| Wisconsin Life Insurance Company, Madison, Wis. | G. G. Stebbins, M. D. |
| Wisconsin National Life Insurance Company, Oshkosh, Wis. | E. B. Williams, M. D. |
| Woodmen of the World Life Insurance Society, Omaha, Neb. | A. D. Cloyd, M. D.<br>H. B. Kennedy, M. D. |

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